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DISTURBANCES OF THE ENDOCRINE BALANCE AND THEIR RELATION TO DISEASES OF METABOLISM *

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LAST year it was my privilege to address the College upon the subject of carbohydrate metabolism and the implications that recent work in this field had upon our knowledge of diabetes mellitus.

Since this address appeared to meet with a certain measure of approval from you, I have ventured this evening to speak again upon certain pieces of work that to my mind are significant to those of us whose interest is concerned with the so-called diseases of metabolism.

It appears to me that it is becoming more and more apparent that the clinical condition that follows hypo- or hyperfunction of an endocrine organ is not merely due to the loss or plethora of that particular internal secretion, but is a result of the disturbance of the normal hormonal equilibrium of the body.

The work of the last few years has shown that the anatomical, and probably to a large extent the functional integrity of the majority of the endocrine organs, is dependent upon the anterior pituitary.

The secretions of this gland either stimulate the production of hormones in the other endocrines or else enable these endocrines to maintain their secreting elements in such a condition that the production of their characteristic hormones becomes possible. There is then, in the truest sense of the word, an interrelationship between the anterior pituitary and the other organs of internal secretion. So widespread is the influence of the anterior pituitary over the whole endocrine system that at the present time it is difficult to consider any glandular interrelationship in which the possible participation of the anterior pituitary must not be allowed for.

Thus it is becoming equally apparent that not only is the destruction of the anterior pituitary followed by a generalized endocrine atrophy, but also that removal of the gonads, thyroid or adrenals is followed by anatomical alterations in the anterior pituitary. These alterations are of such a strik-

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ing character that it is difficult to conceive that they are not attended by equally significant changes in function. If this is so, then myxedema and Addison's disease should be considered not only as conditions dependent upon diminished thyroid or adrenal cortical activity, but also from the point of view that an altered level of anterior pituitary function may be contributing to the clinical condition. In consequence, it becomes of some interest to discuss briefly the effects upon the anterior pituitary of the destruction or removal of the adrenals, thyroid and pancreas.

A. The Adrenal Cortex. Comparatively few observations are recorded upon the effect of adrenalectomy upon the anterior pituitary in animals, and these, probably on account of the stains employed, have yielded but little information. Recently, Crooke,[1] using a modification of the Mallory stain, has carefully studied this organ in 12 authenticated cases of Addison's disease. Not only was the general cytology examined, but in five cases a differential cell count was made. This author finds that the basophiles are greatly reduced in number along with a variable degree of reduction of the acidophiles. These changes were found in one individual even after treatment with cortical extract for 19 months. Crooke has suggested that this loss of basophiles may be associated with the hypoglycemia that is such a constant feature of this disease. This is supported by his later observation that hyperactivity of the basophiles such as is observed in pituitary basophilism is associated with an elevated blood sugar.

In view of the striking alterations induced in the anterior pituitary as a result of destruction of the adrenal cortex it would be surprising if this organ retained its normal degree of function. Grollman's [2] experiments upon adrenalectomized rats maintained with minimal doses of cortical extract indicate that the failure of growth and reproductive function in chronic adrenal insufficiency is due to hypofunction of the anterior pituitary. Such animals will grow again only if given pituitary extracts rich in the growth promoting principles. The injection of potent adrenal cortical extracts is at this time incapable of restoring normal growth. Histological examination of the anterior pituitary of such animals reveals a diminution of both the basophilic and acidophilic cells, the former undergoing the greatest change.

B. The Thyroid. Numerous studies have been carried out upon the changes in the anterior pituitary following thyroidectomy in animals and in cases of human hypothyroidism. Practically all authors are agreed that the acidophiles are greatly reduced, while certain authors have observed alterations in the basophiles. Zeckwer and her co-workers [3] have recently published an excellent paper upon the alterations in the anterior pituitary of young thyroidectomized rats. They find that in all cases where the rats have become stunted in growth the acidophiles had practically disappeared while the basophiles had undergone remarkable changes, becoming enlarged, vacuolated, and containing hyaline material. Zeckwer has made the interesting and probably correct suggestion that the cessation of growth in these young thyroidectomized rats is a consequence of the reduction of the

acidophilic elements of the pituitary. It would be of great interest to know if the administration of anterior pituitary extracts would cause these cretin rats to resume growth.

The above results clearly show that destruction or removal of the adrenals or thyroid causes marked structural alterations in the anterior pituitary. In addition to these anatomical changes evidence is also accumulating that certain aspects of the deficiency, usually attributed to the loss of the thyroid or adrenal secretion, are in reality to be attributed to the concomitant pituitary dysfunction.

Diabetes mellitus is a disease of metabolism that is at present held to be due to hypofunction of the islands of Langerhans. In view of the alterations induced in the anterior pituitary by hypofunction of the adrenals and thyroid it is surprising that so few histological studies of this organ in diabetes have been made. However, Fry [4] and Kraus [5] have reported that following pancreatectomy in animals, or in human diabetics, there is present a proliferation of eosinophiles and an accumulation of colloid material. On the other hand, Warren was unable to confirm such changes in the pituitaries of the diabetics he studied.

There is no doubt, however, of the striking effects of hypophysectomy upon an experimental diabetes, and in view of the bearing of these findings upon the problem of glandular interrelationships and disturbances of the metabolic processes it is necessary to consider in some detail the factors known at present to influence the diabetes of a totally depancreatized animal.

Factors Modifying an Experimental Diabetes

As I pointed out last year, the demonstration by Houssay and Biasotti [6] that hypophysectomy greatly alters the response to total pancreatectomy in animals necessitates a revision of our previous ideas, not only upon the mechanism by which experimental diabetes is produced but also upon the factors normally operating to control the protein, fat and carbohydrate metabolism of the body.

There are three major factors which, when in equilibrium, result in what we speak of as a normal metabolism. These are (*a*) the secretions of the various endocrine organs, (*b*) the liver, and (*c*) the tissues. Disturbance of any of the former such as follows the extirpation of an endocrine organ is followed by a condition in which not only is the metabolic equilibrium disturbed by the loss of this particular secretion, but also by the uncompensated activity of the remaining glands.

The interest excited by the effects of the anterior pituitary hormones upon metabolism should not lead us to neglect the fact that the liver is in all probability the organ upon which their influence is mainly exerted. It is this organ that is the site of glucose formation and probably of the major processes of fat metabolism. Thus, as Mann and Magath,[7] and Yater, Markowitz and Cahoon [8] have shown, removal of the liver even from a

totally depancreatized dog results in a rapid fall of the blood sugar, and Campos [9] has demonstrated that in hepatectomized toads potent anterior pituitary extracts do not exert their usual effect of increasing the blood sugar.

Finally the metabolism of the tissues themselves can be greatly modified by various hormones. Insulin increases their utilization of carbohydrate while epinephrine diminishes it. The effect of the anterior pituitary hormones upon the metabolism of the tissues is a subject which so far has not been investigated. It may well be that one of the factors reducing carbohydrate utilization after pancreatectomy is not entirely the absence of insulin, but is in large part due to the inhibition of glucose oxidation by the pituitary hormones themselves.

Thus it is not surprising that as investigation proceeds a number of conditions are being found by which the usual effects of pancreatectomy can be modified. These can be roughly divided into

(*a*) *Alterations of the endocrine balance*
  (1) Hypophysectomy (Houssay [6])
  (2) Adrenalectomy (Long and Lukens [10])

(*b*) *Disturbances of liver function*
  (1) Complete or partial hepatectomy (Mann and Magath [7])
  (2) Marked fatty infiltration such as follows the giving of low choline diet to a depancreatized animal maintained on insulin (Best et al.[11])

(*c*) *Tissues*
  Reduction of body weight by fasting (Allen [12])

(*d*) *Lesions of the hypothalamus*
  It has been reported by Davis, Cleveland and Ingram [13] that cats depancreatized after placing suitable lesions on the hypothalamic area exhibit a modified diabetes. Whether such lesions exert their effect by interference with the function of the anterior pituitary or whether they interrupt nervous pathways concerned with metabolic processes remains to be decided.

The Relation of the Above Findings to Human Diabetes

In the experimental work cited above the pancreas has been removed before or after the establishment of one of the conditions outlined above. Thus the diabetes studied has been of primary pancreatic origin. It is obvious, however, that the chief interest from a clinical point of view would be in the establishment of the fact that alterations in the functional activity of certain endocrine organs, the liver or central nervous system, could give rise to diabetes mellitus. Now it will be recalled that for many years the view has been held that all cases of diabetes mellitus in man were the result of hypofunction of the islands of Langerhans, and it should also be emphasized that the majority of autopsies upon diabetics disclose pathological

changes in these structures. Nevertheless this unitarian view of the etiology of diabetes in man has not been universally accepted.

Since it has been demonstrated that the removal of the hypophysis or adrenals will modify an existing pancreatic diabetes it is profitable to examine the effects upon carbohydrate metabolism of conditions in which there exists hyperactivity of the anterior pituitary or adrenal cortex.

One of these conditions is acromegaly in which there is present a functioning tumor of the anterior pituitary. In these individuals, as has been repeatedly shown, glycosuria and often frank diabetes are of common occurrence.

Of recent years the extraordinary condition commonly known as " Cushing's syndrome " or pituitary basophilism has received an increasing amount of attention. Although the first cases described by Cushing were associated with a small basophilic adenoma of the anterior pituitary, it is now recognized that in adults the same condition is produced by the presence of an adrenal cortical carcinoma or adenoma. Recently this paradox has been further complicated by the report of three individuals with tumors of the thymus gland who also exhibited this interesting clinical picture.

Lukens and I have examined the records of 20 cases of this syndrome associated with proved basophile adenomas of the pituitary. Of these, 14 exhibited glycosuria. A similar study of 55 cases of proved adrenal cortical tumor or hyperplasia showed that half of them had a demonstrable impairment of carbohydrate tolerance. Finally, all three cases of Cushing's syndrome associated with thymic tumors exhibited glycosuria.

It is obvious from a study of these cases that there exists a generalized glandular derangement, and it is important for an understanding of the glycosuria that is found to investigate what endocrine disturbance is common to these three types of cases. (*a*) In basophilic adenomas of the pituitary hypertrophy of the adrenal cortex, often reaching a marked degree, is common. (*b*) In the cases associated with adrenal cortical tumor or hyperplasia it has heretofore been assumed that the hyperactivity of this organ was responsible for the condition observed. (*c*) In all three reported cases of thymic tumor the adrenal cortex has been enlarged.

These findings, together with the fact that total adrenalectomy is effective in reducing the glycosuria of a depancreatized animal, suggest that the glycosuria observed in the above groups is associated with hyperactivity of the adrenal cortex. Here, however, we cannot rest, since last year Crooke,[14] in an excellent cytological study of the anterior pituitary of six cases of basophilic adenoma, three of adrenal cortical carcinoma and three of thymic tumor, has demonstrated that in all instances the basophile cells were the site of a curious hyaline change. Since this hyaline change is presumably demonstrable in all cases of Cushing's syndrome and since hyperplasia of the adrenal cortex, although very common, is not invariably present, we are forced to conclude that a direct association between hyperactivity of the adrenal cortex and glycosuria has not yet been established.

It may well prove to be that several causes, among them adrenal cortical or thymic hyperactivity, may precipitate this activation of the anterior pituitary. Once this is established a generalized glandular derangement follows, one result of which is glycosuria, and not infrequently clinical diabetes mellitus.

Nevertheless these facts do not answer our original enquiry as to whether individuals without acromegaly or Cushing's syndrome ever develop diabetes mellitus as a consequence of pituitary dysfunction. All the evidence gathered from the effects of various procedures upon experimental diabetes together with that obtained from a study of cases with undisputed pituitary or adrenal dysfunction, although highly suggestive of such an etiology in at least some diabetics, is by no means conclusive. It would, however, appear to offer an advantageous method of approach to the study of the etiological basis of the disease in man.

Factors Determining Glucose Tolerance

Himsworth,[15] in a well documented and ingeniously argued series of papers, has advanced the view: (*a*) That the response of the blood sugar of normal individuals to the ingestion of glucose is determined solely by the carbohydrate content of the diet previous to the test. With a low carbohydrate diet the curves indicate a decreased tolerance to ingested glucose, but as the proportion of dietary carbohydrate is increased, curves indicative of an improving glucose tolerance are obtained. (*b*) The sensitivity of the individual to a given amount of insulin increases with the amount of carbohydrate in the diet. (*c*) It is commonly assumed that when glucose is ingested the supply of insulin is temporarily increased to meet this circumstance. Himsworth points out that this supposition is unnecessary since his work indicates that increasing the amount of carbohydrate in the diet increases the efficiency of the usual supply of insulin to such an extent that the additional carbohydrate is easily disposed of. In consequence it is unnecessary to postulate variations in insulin secretion in response to carbohydrate ingestion. As will be seen shortly, Soskin et al.,[16] from an entirely different type of experiment, have arrived at similar conclusions. These views are of course at variance with those of other workers, particularly Zuntz and LaBarre,[17] and it would appear that the stage is set for a controversy similar to that waged over the continuous or intermittent secretion of epinephrine. (*d*) Of even greater interest are Himsworth's views as to the reason for the greater efficiency of insulin when a large amount of carbohydrate is being ingested. He has advanced the hypothesis that insulin as secreted by the pancreas is physiologically inactive and requires the presence of an activator, probably supplied by the liver, in order to bring out its well known effects upon carbohydrate utilization. He implies that a large carbohydrate intake favors the production of the "activator" while low carbohydrate diets inhibit its production. Now it will be apparent that if

this view is correct, diabetes could occur in an individual with a normal insulin supply as a result of a deficient quantity of insulin activator.

On the basis of this hypothesis, Himsworth has attempted to classify human diabetes into two groups: (*a*) insulin sensitive, and (*b*) insulin insensitive. The former are those in whom a deficiency of insulin production by the pancreas is the essential defect. These individuals are those in whom injected insulin is highly effective, and furthermore are the group of diabetics who are most likely to tolerate a high carbohydrate-low fat diet without any increase in insulin requirements.

The insulin insensitive group, on the other hand, are those individuals who will not tolerate an increase in carbohydrate intake unless the insulin supply is correspondingly increased. Himsworth believes that the insulin insensitive group of diabetics are those in whom insulin deficiency is not the primary cause of the disease, but are diabetic because of a deficiency of some substance which in normal individuals is essential for the proper action of insulin.

Soskin and his co-workers,[16] although in agreement with Himsworth that the pancreas does not secrete an increased amount of insulin after glucose ingestion, disagree with him upon the question as to whether insulin requires to be activated before it becomes physiologically effective in the body.

These workers hold that when the blood sugar level falls below a certain value the formation of glucose in the liver from non-carbohydrate sources (gluconeogenesis) is stimulated, and conversely, when the blood sugar level rises above a certain point, the amount of gluconeogenesis is decreased. Furthermore, it is held that this capacity of the liver to regulate the formation of glucose in accordance with the needs of the body is normally under the control of the opposing influences of the hormones of the pancreas and hypophysis. Their experimental work has led them to the conclusion that the variable factor in this endocrine balance is not the supply of pancreatic insulin but the amount of liver gluconeogenesis and consequently the amount of hypophyseal activity. Therefore, when glucose is ingested the ensuing changes in the blood sugar curve are not the result of an increased secretion of insulin, but are determined by alterations in the amount of glucose formation by the liver.

When this hypophyseal-pancreas-liver relationship is disturbed by pancreatectomy, then excessive gluconeogenesis continues during glucose ingestion and a diabetic tolerance curve results; conversely, when the hypophysis is removed, the marked decrease in the gluconeogenetic processes renders the organism insulin sensitive and increases the tolerance to glucose. When both pancreas and hypophysis are excised an intermediary level is established at which point " normal " tolerance curves may be found.

In view of this work, along with that of Houssay and others, it appears that other reasons than lack of an insulin activator might be ascribed to cases of insulin-insensitive diabetes. Thus it has been established (*a*) that hypo-

physectomized animals are insulin sensitive, (*b*) such animals have an increased carbohydrate tolerance, (*c*) normal animals may be rendered insulin insensitive by the injection of anterior pituitary extracts even though the composition of the diet remains unchanged, and (*d*) such injections decrease their carbohydrate tolerance. Therefore, instead of invoking a hypothetical insulin activator, is it not more reasonable to say that the anterior pituitary hormones play a conspicuous rôle in determining the response of the organism not only to ingested carbohydrate, but also to exogenous and endogenous insulin?

It may thus be postulated that Himsworth's insulin sensitive group of diabetics are those (as he himself has pointed out) in whom the defect is an inadequate supply of insulin, while the insulin insensitive group are those diabetics in whom a relative preponderance of hypophyseal activity is the exciting cause of the disease even though their supply of pancreatic insulin remains within normal limits.

I wish, however, to emphasize that no experimental work supporting a classification of diabetes along these lines has yet appeared, nor has any evidence yet been adduced that in certain diabetics the hypophyseal or adrenal function is deranged.

The interest of these experiments, apart from the fact that they ascribe an extra-pancreatic origin to certain cases of diabetes, lies in the concept that the response of the organism to such a physiological process as the ingestion of carbohydrate is determined not by the liver, pancreas or tissues acting alone, but by a response that necessitates the readjustment of an equilibrium that is normally maintained by the activity of the endocrine organs. This, of course, is merely a restatement of the principle of homeostasis that the work of Cannon [18] has done so much to disclose.

Long continued disturbances of this equilibrium such as are induced by chronic hyper- or hypofunction of one or more endocrine organs, result in conditions which are clinically spoken of under such names as Graves' disease or Addison's disease. While it is obvious that acute deprivation of any particular hormone may result in death before any secondary consequences can be established, this is not the condition that is usually encountered in man.

It is my belief that a better understanding of the diseases of metabolism that are associated with a disturbed endocrine function can be reached by ceasing to regard them merely as an expression of the effects of alterations in function limited to one endocrine organ, but rather in the light of our newer knowledge of the close interrelationship between all the organs of internal secretion.

These remarks should not be interpreted as endorsing ill-timed surgical assaults upon the pituitary and adrenals either in the case of hyperthyroidism or diabetes mellitus, since as I have previously pointed out, no evidence is yet available that these organs are primarily involved in the appearance of these diseases in man.

BIBLIOGRAPHY

1. Crooke, A. C., and Russell, D. S.: The pituitary gland in Addison's disease, Jr. Path. and Bact., 1935, xl, 255.
2. Grollman, A., and Firor, W. M.: Rôle of the hypophysis in experimental chronic adrenal insufficiency, Am. Jr. Physiol., 1935, cxii, 310.
3. Zeckwer, I., Davison, L. W., Keller, T. B., and Livingood, B. S.: The pituitary in experimental cretinism. I. Structural changes in the pituitaries of thyroidectomized rats, Am. Jr. Med. Sci., 1935, cxc, 145.
4. Fry, H. J. B.: The pituitary gland in diabetes mellitus and disorders of the glands of internal secretion, Quart. Jr. Med., 1915, viii, 277–299.
5. Kraus, E. J.: Hypophyse und Diabetes mellitus, Virchow's Arch. f. path. Anat., 1920, ccxxviii, 68–133.
6. Houssay, B. A., and Biasotti, H.: Hypophysis, carbohydrate metabolism and diabetes, Endocrinology, 1931, xv, 511.
7. Mann, F. C., and Magath, T. B.: The effect of removal of the liver after pancreatectomy on the blood sugar level, Arch. Int. Med., 1923, xxxi, 797.
8. Yater, W. M., Markowitz, J., and Cahoon, R. F.: Consumption of sugar by muscle in the non-diabetic and diabetic state, Arch. Int. Med., 1933, li, 800.
9. Campos, C. A., Curutchet, J. L., and Lanari, A.: Rôle du foie dans l'action diabétogène du lobe glandulaire de l'hypophyse de crapaud, Compt.-rend. Soc. de biol., 1933, cxiii, 467.
10. Long, C. N. H., and Lukens, F. D. W.: The effect of adrenalectomy and hypophysectomy upon experimental diabetes in the cat, Jr. Exper. Med., 1936, lxiii, 465.
11. Best, C. H., Ferguson, G. C., and Hershey, J. M.: Choline and liver fat in diabetic dogs, Jr. Physiol., 1933, lxxix, 94.
12. Allen, F. M.: Glycosuria and diabetes, 1913, Harvard University Press.
13. Davis, L., Cleveland, D., and Ingram, W. R.: Effect of hypothalamic lesions and stimulation of autonomic nervous system upon carbohydrate metabolism, Arch. Neurol. and Psychiat., 1935, xxxiii, 592.
14. Crooke, A. C.: A change in the basophile cells of the pituitary common to conditions which exhibit the syndrome attributed to basophile adenoma, Jr. Path. and Bact., 1935, xli, 339.
15. Himsworth, H. P.:
    (*a*) Physiological activation of insulin, Clin. Sci., 1933, i, 1.
    (*b*) Dietetic factors influencing glucose tolerance and activity of insulin, Jr. Physiol., 1934, lxxxi, 29.
    (*c*) Influence of diet on sugar tolerance of healthy men and its reference to certain extrinsic factors, Clin. Sci., 1934, i, 251.
    (*d*) Dietetic factor determining glucose tolerance and sensitivity to insulin of healthy men, Clin. Sci., 1935, ii, 67.
    (*e*) Diabetes mellitus: its differentiation into insulin-sensitive and insulin-insensitive types, Lancet, 1936, ccxxx, 127.
16. Soskin, S., Allweiss, M. D., and Cohn, D. J.: Influence of the pancreas and the liver upon the dextrose tolerance curve, Am. Jr. Physiol., 1934, cix, 155.
17. Zuntz, E., and LaBarre, J.: Sur l'augmentation de la teneur en insuline du sang veineux pancréatique après l'hyperglycémie provoquée par injection de glucose, Compt.-rend. Soc. d. biol., 1927, xcvi, 421.
    Sur la sensibilité des centres nerveux supérieurs à l'hyperglycémie provoquée par l'injection de dextrose, Compt.-rend. Soc. d. biol., 1927, xcvi, 1400.
18. Cannon, W. B.: Stresses and strains of homeostasis, Am. Jr. Med. Sci., 1935, clxxxix, 1.

A COMPARISON OF THE EFFECTIVENESS OF GLUTAMIC ACID HYDROCHLORIDE AND DILUTE HYDROCHLORIC ACID AS THE REPLACEMENT THERAPY IN ANACIDITY MEASURED BY FRACTIONAL GASTRIC ACID TITRATION AND HYDROGEN-ION CONCENTRATION CURVES *

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For the most part, anacidity has been regarded an interesting but scarcely serious medical curiosity. In the absence of gastric carcinoma, or of blood changes suggestive of Addisonian anemia, little consideration has been generally given the anacidity. In fact, since the work of Castle,[1] it has progressively diminished in importance as a factor in anemia. Clinically, spectacular therapeutic results have been obtained from the administration of hydrochloric acid for the relief of vague, but distressing, digestive symptoms, or in the more obvious gastrogenous diarrhea. Experimentally, time and effort have been lavished upon the study of the response of the achlorhydric to histamine and to the ability of the anacid stomach to secrete parenterally injected neutral red, but small thought indeed has been given to the possibility of a far-reaching and insidious effect of anacidity upon the body's physiology.

Numerous papers have pointed out the relatively higher incidence of anacidity in cholecystitis, diabetes, arthritis, and their like, but the likelihood of anacidity being cause rather than effect has gone almost completely unsuspected. We believe this relationship will become evident when the physiology of the upper small intestine is completely understood.

Scattered evidence is now available, and more is certain to be added, to show that the duodenum is rivalled only by the pituitary as the source for a multiplicity of hormones with many, and extended, physiological effects. Further, the trigger that sets this off is the arrival of the gastric hydrochloric acid into the duodenum. We attribute this action to the hydrochloric acid as the intrinsic agent. It is not, however, the sole agent capable of inaugurating the reaction, for any substance that can alter the osmotic conditions in the duodenum away from isotonicity will activate the duodenal mucosa to a greater, or a lesser, degree.

Forgetting for a moment the action of the gastric hydrochloric acid in initial protein digestion, or as a bactericide, let us examine the part it might play upon its entrance into the duodenum. We need only recall its rôle in

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the crucial experiment of Bayliss and Starling,[2] using the denervated isolated jejunal loop to demonstrate the hormonal mechanism for the external secretion of the pancreas. Gastric hydrochloric acid as the intrinsic agent supplying the stimulus in the duodenum and upper jejunum in the production of a substance capable of diminishing the blood-sugar concentration, has been suggested since the work of Freud and Saadi-Nazim[3] in dogs in 1926. Whether this is due to another hormone which stimulates the pancreatic islets, or whether hydrochloric acid itself is able to modify a raised blood-sugar level, or whether both mechanisms are operative is, so far, not entirely clear. We are about to publish data which demonstrate this mechanism for man and which indicate the separate action rather than the islet stimulation. In his discovery of cholecystokinin, Ivy[4] has shown the relationship of the gastric acid to gall-bladder emptying. Recently, we[5] demonstrated the importance of the same acid as the intrinsic agent in the duodenum which acts as the control of the local mechanism concerned with gastric evacuation. It is also likely from our studies of the motor function of the resected stomach[6] that the gastric motor inhibitory hormone conceived in the work of Farrell and Ivy,[7] Lim,[8] Quigley,[9] and their co-workers is dependent for its intrinsic motivation upon the hydrochloric acid of the stomach. The importance of this acid in the absorption of calcium from the intestine was recently graphically demonstrated by Ivy[10] in the bone changes produced in young and adult dogs after gastrectomy.

Thus, because of the manifold and extended effects of which it is possibly the source, anacidity demands more interest than a cursory one in its etiology and in its replacement therapy—which is for the present quite simply, the attempt to simulate as accurately as possible a normal gastric acid curve.

Method

Fourteen patients with anacidity were studied. Nine remained anacid after histamine. Fractional gastric analysis was used throughout. The patients reported after an overnight fast. The fasting gastric contents were removed through a Rehfuss tube, and then the test meal, which consisted of 20 grams of zweiback and 300 c.c. of distilled water, was ingested. The gastric response to this meal was first determined, specimens being removed at quarter-hour intervals for two hours, or until the stomach was empty. Each specimen was titrated for free acid to dimethylamidoazobenzol and for total acid to phenolphthalein; and recorded in the usual manner in c.c. of tenth normal acid per 100 c.c. of gastric contents. Hydrogen-ion concentration was determined with the quinhydrone electrode.

The same patients were then studied after addition of varying amounts of dilute hydrochloric acid to the water before ingestion of the meal. A dropper was used for measuring the acid in order more closely to simulate the clinical method of administration. This dropper yielded 16 drops to the c.c. Glutamic acid and glutamic acid hydrochloride were administered

in capsules (0.31 gram each) in two portions; one-half when half the test was taken, and the other half at the end of the meal. Extractions and determinations were carried out as with the zwieback-and-water meal. One hundred and four fractional analyses were made on the 14 patients.

Discussion

Replacement therapy in anacidity has pretty generally taken the form of hydrochloric acid. Some years ago, Arthur F. Hurst [11] recognized the inadequacy of the official pharmacopoeial dosage and advocated quantities of 4 to 6 c.c. which was, and still is, considered by many to be a radical recommendation. Later, Crohn,[12] and Kern, Rose, and Austin [13] demonstrated the failure of the usual therapeutic doses of dilute hydrochloric acid to modify intragastric acidity in achlorhydria. Superficially the usual doses are found to be therapeutically efficient, but when measured by actual titration and hydrogen-ion determinations in fractional gastric studies, it is surprising to see how ineffective massive doses are to establish even an approach

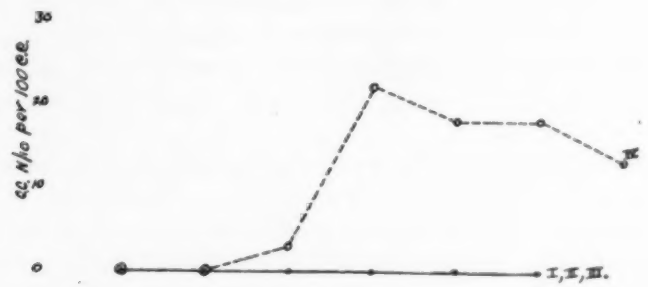


Chart 1. Case S. L. I. Free acid titration curve after Ewald meal. II. Free acid titration curve after Ewald meal plus 80 drops dilute HCl. III. Free acid titration curve after Ewald meal plus 4 capsules glutamic acid. IV. Free acid titration curve after Ewald meal plus 4 capsules glutamic acid HCl.

to what would be considered a normal gastric acid response. (See charts.) An amount of hydrochloric acid as large as 120 to 160 drops (7.5 to 10.0 c.c.) added to the Ewald meal (charts 5 and 7) produced a low free acid curve during the fractional analysis, while 80 drop portions (5 c.c.) were usually inadequate to show any free acid to Töpfer's reagent at any time (charts 1, 5, and 7). The results obtained in the hydrogen-ion concentration curves confirmed the titration values insofar as the addition of smaller quantities of the acid to the meal failed to produce a pH reading below 3.5, at which point free acid will be demonstrated by Töpfer's reagent. (Charts 3, 4, and 7.) (In several thousand pH determinations on gastric samples with the quinhydrone electrode, we have always obtained a free acid reaction to Töpfer's when the pH reading was below 3.5.) It would appear, therefore, that the therapeutic effects derived from the administration of the usual dosage of hydrochloric acid are definitely not dependent upon the

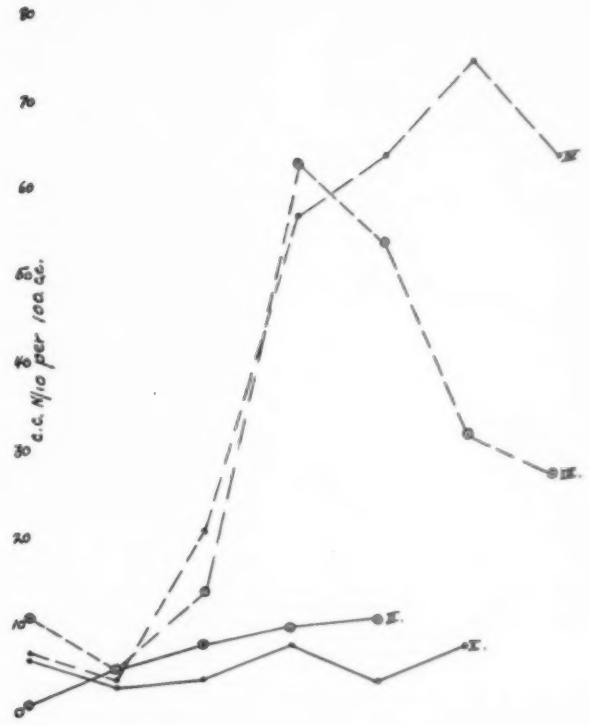


CHART 2. Case S. L. I. Total acid titration curve after Ewald meal. II. Total acid titration curve after Ewald meal plus 80 drops dilute HCl. III. Total acid titration curve after Ewald meal plus 4 capsules glutamic acid. IV. Total acid titration curve after Ewald meal plus 4 capsules glutamic acid HCl.

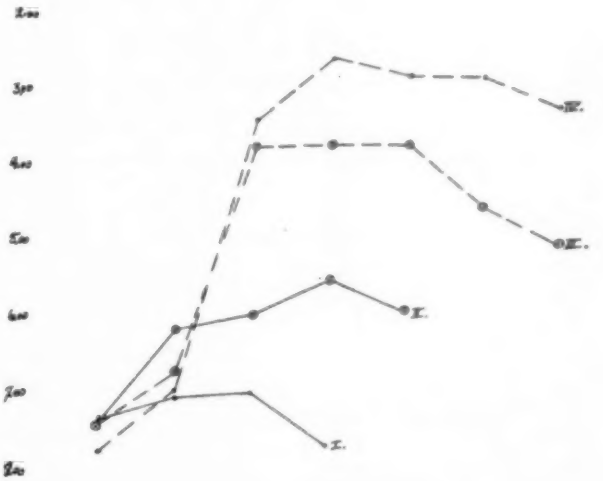


CHART 3. Case S. L. I. Curve of pH after Ewald meal. II. Curve of pH after Ewald meal plus 80 drops dilute HCl. III. Curve of pH after Ewald meal plus 4 capsules glutamic acid. IV. Curve of pH after Ewald meal plus 4 capsules glutamic acid HCl.

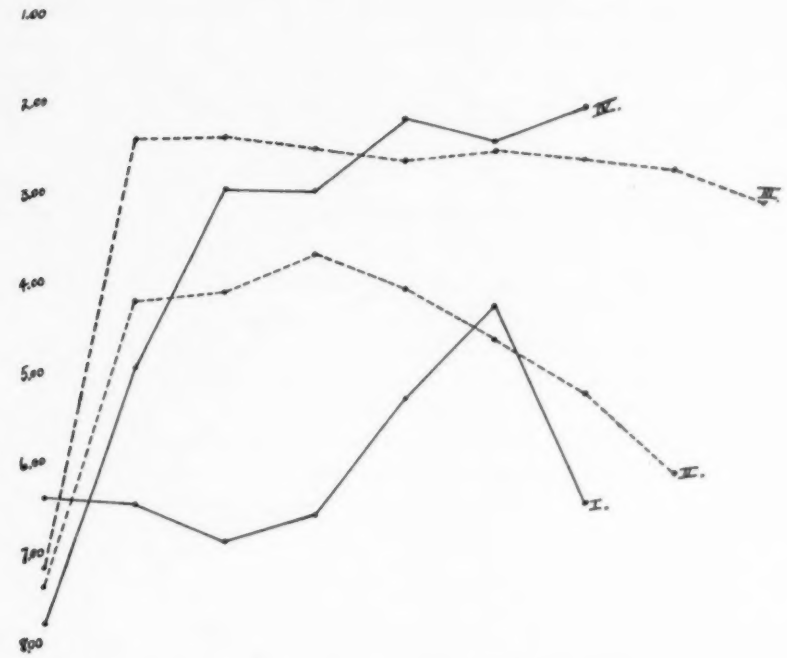


CHART 4. Case L. F. I. Curve of pH after Ewald meal. II. Curve of pH after Ewald meal plus 80 drops dilute HCl. III. Curve of pH after Ewald meal plus 160 drops dilute HCl. IV. Curve of pH after Ewald meal plus 4 capsules glutamic acid HCl.

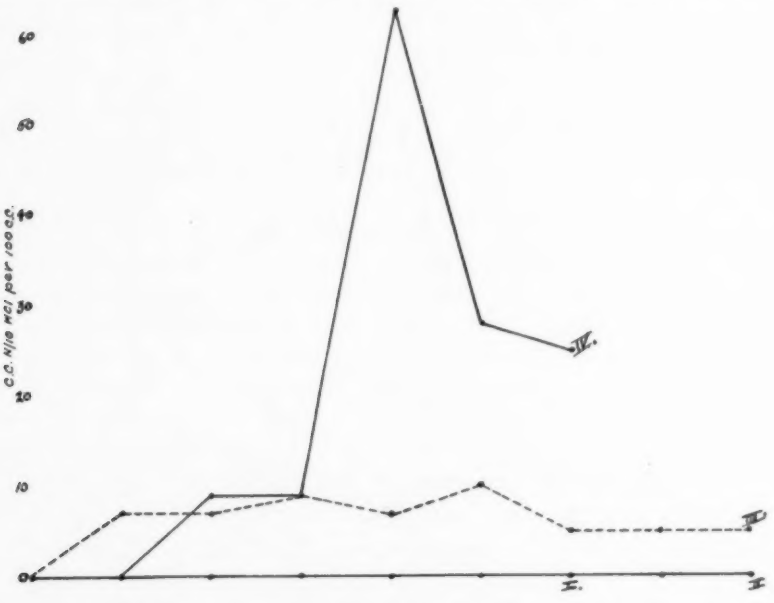


CHART 5. Case L. F. I. Free acid curve after Ewald meal. II. Free acid curve after Ewald meal plus 80 drops dilute HCl. III. Free acid curve after Ewald meal plus 160 drops dilute HCl. IV. Free acid curve after Ewald meal plus 4 capsules glutamic acid HCl.

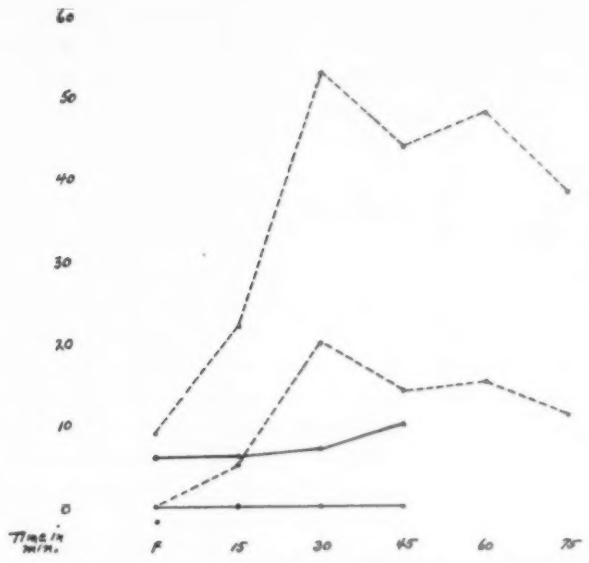
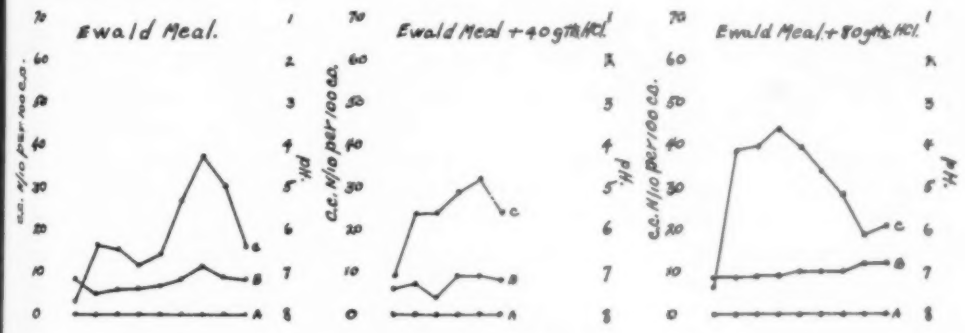


CHART 6. Case M. M. F. ——— Free and total acid curve after Ewald meal + 60 drops dilute HCl. - - - - - - Free and total acid curve after Ewald meal + 2 capsules glutamic acid HCl.



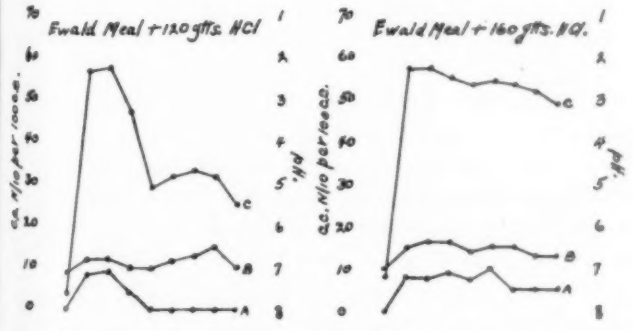


CHART 7. A = curve of free HCl. B = curve of total acidity. C = curve of pH.

presence in the stomach of any free acidity at the time of digestion. From our experiences with the rôle of the hydrochloric acid in the duodenum, we venture the opinion that the beneficial clinical results are caused by the altered osmotic conditions produced in the upper intestine by the administered acid.

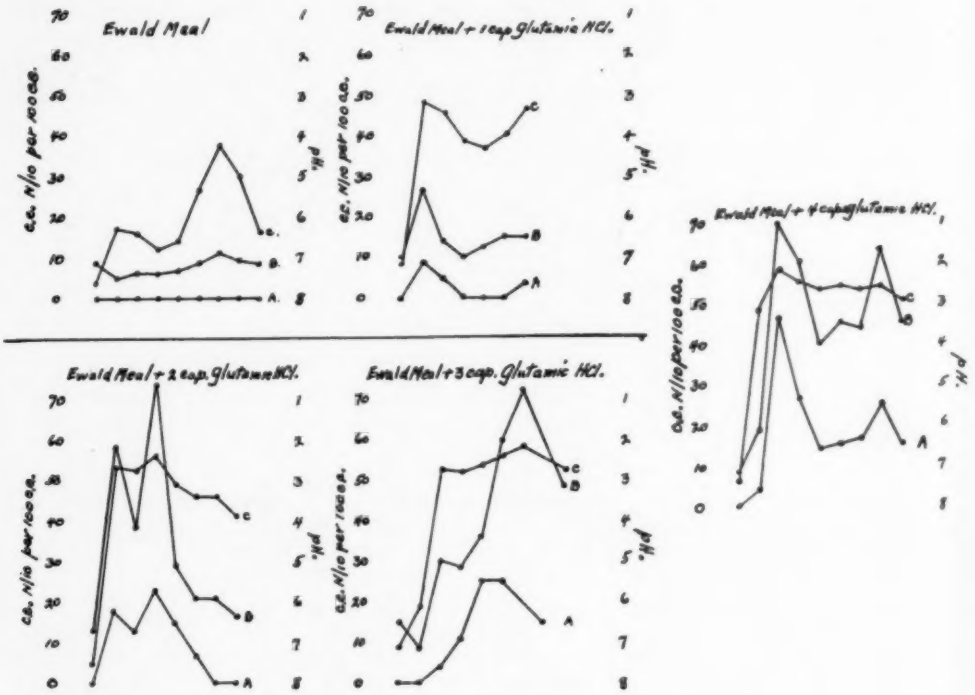


CHART 8. A = curve of free HCl. B = curve of total acidity. C = curve of pH.

GLUTAMIC ACID HYDROCHLORIDE

Glutamic acid (a-amino-glutaric acid) was isolated by Ritthausen [14] in 1869 from vegetable proteins by acid hydrolysis. It is very probably one of the essential amino acids, and in 1913 Abderhalden [15] determined that it was a constituent of normal blood. Ikeda [16] isolated the acid from a Japanese seaweed to which it gives its peculiar flavor. Moreover, in Japan it has for some time been used as a seasoning for foods, and in that country the use of the sodium salt—the most useful of the non-poisonous metallic radicals—has become widespread. Newburgh and Marsh [17] studying the toxic effects of amino acids established that doses of glutamic acid as large as two grams per kilogram body weight, when injected into rabbits and puppies, gave no evidence of renal injury. Tagawa [18] considers glutamic acid a physiological protein decomposition product which, like meat extracts, has the ability strongly to stimulate hydrochloric acid secretion, while secre-

tion by the stomach is still possible. In the metabolism of glutamic acid, cognizance must be taken of the fact that three of its carbon atoms enter into the formation of glucose.[19] This, according to Ringer, Frankel and Jonas,[20] takes place by way of succinic acid.

Combined with hydrochloric acid to form a white powder, glutamic acid lends itself to easy administration in capsule form. Recently, von Bergmann [21] recommended its use in anacidity, and Mahler [22] studied its effect, in the form of muripsin (glutamic acid hydrochloride and pepsin), on both the gastric chemistry and on the appearance of the gastric mucosa through the gastroscope. Mahler found that even in large dosage, it produced no hyperemia. We have done comparative studies with glutamic acid hydrochloride,* and with varying quantities of the official dilute hydrochloric acid. In contact with water, the combination is readily broken up, and the hydrochloric acid liberated. Considering that glutamic acid hydrochloride was one of the first amino acid salts to be isolated in pure form (Hlasiwetz and Habermann [23] in 1873), it is indeed surprising that it did not find its way much earlier into the replacement therapy of anacidity.

If we take the titration and hydrogen-ion concentration figures as seen in the charts 1 to 8 as a measure of the effectiveness of the replacement therapy in anacidity, the superiority of glutamic acid hydrochloride over the official dilute hydrochloric acid is obvious. With relatively small amounts of this combination, a close parallelism of the gastric acid curve in the achlorhydric with that which would be the response in the normal acid stomach to the usual Ewald test meal can be seen—a simulation not achieved even with enormous doses of the official hydrochloric acid solution.

At times we obtained titration figures, especially after the larger doses of the glutamic acid, which are normally never seen in the gastric juice. These were probably caused by a portion of the ingested drug which had not been mixed with the gastric contents. Charts 6, 7, and 8 also demonstrate the marked difference between free and total acid titration, following the use of glutamic acid hydrochloride. This is probably due to the glutamic acid content.

We have attempted to determine the approximate equivalent of the glutamic acid hydrochloride in terms of dilute hydrochloric acid both in vitro and in vivo. Table 1 represents the titration and pH figures of varying amounts of dilute hydrochloric acid, glutamic acid, and glutamic acid hydrochloride, each dissolved in 100 c.c. of distilled water. Titration was done to pH 7.4 using a comparator block and phenol red as indicator. Hydrogen-ion concentration was determined with the quinhydrone electrode. It will be noted that solutions of glutamic acid alone were included only up to three capsules (0.93 gr.), since that represented the degree of solubility of that acid in 100 c.c. of water.

In vitro experiments showed the titration figure of the contents of one

* Glutamic acid hydrochloride was kindly supplied by the Calco Chemical Company, Inc., for these investigations.

TABLE I

Dissolved in 100 c.c. distilled H_2O	Titration to pH 7.4 (c.c. N/10 per 100 c.c.)	pH
10 drops dil. HCl (U. S. P.)	16.3	1.85
1. cap. glutamic acid	17.0	3.23
1 cap. glutamic HCl	34.3	2.14
20 drops dil. HCl	31.9	1.57
2 cap. glutamic acid	34.1	3.20
2 cap. glutamic HCl	68.7	1.92
30 drops dil. HCl	46.1	1.41
3 cap. glutamic acid	45.5	3.19
3 cap. glutamic HCl	101.0	1.85
40 drops dil. HCl	64.3	1.27
4 cap. glutamic acid	Not completely soluble	
4 cap. glutamic HCl	133.5	1.76
60 drops dil. HCl	98.6	1.11
6 cap. glutamic HCl	202.0	1.67
80 drops dil. HCl	132.5	1.00
8 cap. glutamic HCl	270.7	1.58

capsule of glutamic acid hydrochloride to be equivalent to about 20 drops of dilute hydrochloric acid, or equivalent to one capsule of glutamic acid (0.31 gm.) plus 10 drops of dilute hydrochloric acid. The titration of larger amounts of the glutamic acid hydrochloride bear out this relationship. Yet in vivo the effectiveness of the glutamic acid hydrochloride in altering the intragastric reaction is far greater than its equivalent in vitro titration would indicate (charts 7 and 8).

If then the intragastric effects are to be considered a measure of the therapeutic efficiency, one capsule (0.31 gr.) of the glutamic acid hydrochloride appears to be as effective as a massive dose of the dilute hydrochloric acid. If to this greater ability to alter the gastric chemistry is added the ease of administration and the elimination of the unpleasant mouth effects of the official acid, we have in glutamic acid hydrochloride a highly desirable addition to the replacement therapy of anacidity. In one patient we noticed that considerable bladder irritation and frequency produced when adequate dosage of the official acid was administered to control a gastrogenous diarrhea were entirely relieved when glutamic acid hydrochloride was substituted. Clinically we have obtained satisfactory results from the administration of one capsule (0.31 gr.) of the glutamic acid hydrochloride shortly after the beginning of the meal, and another capsule at the completion of the meal.

SUMMARY AND CONCLUSIONS

The problem of anacidity has been subjected to rather one-sided investigation, and achlorhydria and its relation to duodenal function carries many implications which have thus far been overlooked. Gastric hydrochloric acid is the intrinsic agent which upon its arrival into the duodenum

originates the production or liberation of a group of hormones that have far-reaching physiological effects; and this gives to replacement therapy a greater significance than the mere relief of vague digestive symptoms or of a gastrogenous diarrhea. The inadequacy of the official dilute hydrochloric acid, even in massive doses, to alter gastric chemistry is illustrated by fractional gastric analyses, both by acid titration and hydrogen-ion determinations. The marked superiority of glutamic acid hydrochloride in relatively small dosage over the dilute hydrochloric acid is similarly demonstrated, as well as its advantages in administration.

In all, 104 gastric studies were made on 14 cases of achlorhydria, nine of whom had shown no response to histamine injection. The charts used for illustrations were selected from this group.

BIBLIOGRAPHY

1. Castle, W. B., Heath, C. W., and Strauss, M. B.: Observations on the etiologic relationship of achylia gastrica to pernicious anemia. IV. A biologic assay of the gastric secretion of patients with pernicious anemia having free hydrochloric acid and that of patients without anemia or with hypochromic anemia having no free hydrochloric acid and of the rôle of intestinal permeability to hemopoietic substances in pernicious anemia, Am. Jr. Med. Sci., 1931, clxxxii, 741.
2. Bayliss, W. M., and Starling, E. H.: The mechanism of pancreatic secretion, Jr. Physiol., 1902, xxviii, 325.
3. Freud, J., and Saadi-Nazim: Action des injections intra-duodénales d'acide sur la sécrétion interne du pancréas, Compt.-rend. Soc. de biol., 1926, xcv, 571.
4. Ivy, A. C.: Factors concerned in the evacuation of the gall-bladder, Medicine, 1932, xi, 345.
5. Shay, H., and Gershon-Cohen, J.: Experimental studies in gastric physiology in man. II. A study of pyloric control; the rôles of acid and alkali, Surg., Gynec. and Obst., 1934, lviii, 934.
6. Shay, H., and Gershon-Cohen, J.: Experimental studies in gastric physiology in man. IV. The motor function of the resected stomach, Am. Jr. Digest. Dis. and Nutr., 1935, ii, 608.
7. Farrell, J. I., and Ivy, A. C.: Studies on the motility of the transplanted gastric pouch, Am. Jr. Physiol., 1926, lxxvi, 227.
8. Lim, R. K. S., Loo, C. T., and Liu, A. C.: Observations on the secretion of the transplanted stomach, Chinese Jr. Physiol., 1927, i, 51.
9. (a) Quigley, J. P., Zettleman, H. J., and Ivy, A. C.: Analysis of the factors involved in gastric motor inhibition by fats, Am. Jr. Physiol., 1934, cviii, 643.
   (b) Quigley, J. P., and Phelps, K. R.: The mechanism of gastric motor inhibition from ingested carbohydrates, Am. Jr. Physiol., 1934, cix, 133.
10. Ivy, A. C.: In Discussion at Meeting of American Gastroenterological Association in June, 1935, to be published in American Journal of Digestive Diseases and Nutrition.
11. Hurst, A. F.: Achlorhydria: its relation to pernicious anemia and other diseases, Lancet, 1923, i, 111.
12. Crohn, B. B.: Studies in fractional estimation of stomach contents. III. Effects of hydrochloric acid therapy on the acid titer of the stomach during digestion, Am. Jr. Med. Sci., 1918, clvi, 656.
13. Kern, R. A., Rose, E., and Austin, J. H.: Effect of orally administered hydrochloric acid upon gastric contents in normal individuals and in patients with achlorhydria, Jr. Clin. Invest., 1926, ii, 545.

14. RITTHAUSEN, H.: Asparaginsäure und Glutaminsäure, Zersetzungsprodukte des Legumins und Conglutins beim Kochen mit Schwefelsäure, Jr. f. prakt. Chem., 1869, cvii, 218.
15. ABDERHALDEN, E.: Der Nachweis von freien Aminosäuren im Blute unter normalen Verhältnissen, Ztschr. f. physiol. Chem., 1913, lxxxviii, 478.
16. IKEDA, K.: On the taste of the salts of glutamic acid, Eighth International Congress of Applied Chemistry, 1912, xviii, 147.
17. NEWBURGH, L. H., and MARSH, P. L.: Renal injuries by amino acids, Arch. Int. Med., 1925, xxxvi, 682.
18. TAGAWA, J.: Über die Magensekretionerregendes Wirkung der Salzsäuren Aminosäuren, Biochem. Ztschr., 1931, ccxliii, 330.
19. LUSK, G.: The production of sugar from glutamic acid ingested in phlorhidzin glycosuria, Am. Jr. Physiol., 1908, xxii, 174.
20. RINGER, A. I., FRANKEL, E. M., and JONAS, L.: The chemistry of gluconeogenesis. IV. The fate of succinic, malic and malonic acids in the diabetic organism, with consideration of the intermediary metabolism of aspartic and glutamic acids, proline, lysine, arginine and ornithine, Jr. Biol. Chem., 1913, xiv, 541.
21. VON BERGMANN, G.: Die Bedeutung der Anazidität des Magens und einer Ausreichenden Substitutionstherapie, Deutsch. med. Wchnschr., 1933, lix, 1, 44.
22. MAHLER, P.: Über die Beeinflussung der Magensaftsekretion durch kombinierte Salzsäure und Glutaminsäuretherapie, Med. Klin., 1933, xxix, 943.
23. Quoted by Mahler.[22]

THE MEDICAL AND ECONOMIC ADVANTAGES OF ROENTGENOGRAPHIC CHEST SURVEY OF ALL HOSPITAL ADMISSIONS *

By Fred Jenner Hodges, M.D., *Ann Arbor, Michigan*

Few radiographic procedures lend themselves more readily to routine mass application than simple postero-anterior filming of the chest. Other than removal of clothing above the waist-line no advance preparation of the patient is necessary. Great speed without sacrifice of quality can be attained in handling patients because positioning is simple and exposure time is measured in split seconds. Photographic processing in volume offers no serious problem.

Roentgenographic examination of the chest provides a wealth of detailed information concerning the thorax and its contents unrivaled by any other method of approach. The finished film serves furthermore as a valuable objective record which may be preserved for future reference. Even those roentgenograms presenting no recognizable abnormality become valuable as controls against which later chest changes may be contrasted. The predominance of requests for roentgen-ray consultations in which chest examination is required among all of the numerous procedures employed by the roentgenologist bespeaks the soundness of this contention.

It is by no means an uncommon experience to find roentgen-ray evidence of extensive pulmonary or mediastinal disease in the face of negative or inconclusive physical findings. Such findings, furthermore, may be associated with no suggestive symptoms. Purely upon the basis of such reasoning there seems to be no valid reason for withholding the benefits to be derived from this simple procedure from any patient seeking medical advice.

There is one possible reason, however, the validity of which need scarcely be urged; namely, prohibitive cost; cost not only to the person who must pay the material roentgen-ray expense as well as the professional fee for interpretation but, in addition, the initial investment cost to the hospital, clinic, or private practitioner of roentgenology. In order to test the actual value of routine roentgen-ray chest survey and to determine whether or not the cost need necessarily prove prohibitive, all patients registering in the University Clinic, both the hospital and out-patient groups, during the period from June 27 to July 13, 1935 inclusive, were so examined. It was recognized in advance that there could be no prospect of a permanent institution of the plan unless it could be shown that it could justify itself amply in the matter of medical value and at the same time prove itself to be self-supporting without imposing financial hardship upon registering patients. Before

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the test was begun it was decided that unless the following benefits could be demonstrated the plan could not hope to become permanent:

1. Increased diagnostic accuracy.
2. Increased diagnostic speed.
3. Economy for the patient (lowered aggregate roentgen-ray cost to group).
4. Economy for the institution (increased speed in clearing patients; no loss of revenue in Department of Roentgenology).
5. Increased availability of roentgenological service to entire patient group by spread of cost.

Physical Facilities and Method of Procedure

In order that patients might be examined with greatest possible dispatch and the minimum inconvenience, apparatus was set up in a small room 12′ by 12′, immediately adjoining the room in the registration department where blood samples are routinely taken for serological examination. Seven temporary dressing rooms were erected in the corridor as well as a small, light-proof film loading room. To insure roentgenograms comparable to those made with the regular chest apparatus in the roentgen-ray department, a machine was installed capable of producing satisfactory exposures at six foot distance in 1/50 second. High speed of exposure furthermore eliminated the necessity for rigid fixation of the patient. A technician was provided throughout registration hours as well as a ward helper to attend patients. Stock celluloid films of 14 by 17 size were used rather than less costly paper, again in order to maintain uniformity of roentgenographic quality as well as to permit photographic processing with existing facilities. All films were developed during the night by a second technician employed for that purpose to avoid crowding in the roentgen-ray dark room. All films were identified photographically with date and a serial number which last was entered upon a card bearing a duplicate imprint of the patient's admission data. When processed, all films were stored for three months, unread, in order that the immediate results of the test might not alter the regular handling of the patient and to permit ultimate disposal of the cases without bias. At the end of the three month period all films were read in unbroken sequence by the assembled staff of the Roentgenology Department. Diagnostic statements were recorded in accordance with a prearranged code designed to permit direct transfer to punch cards for mechanical sorting (table 1). In addition to diagnostic material, such information as age, sex, race, service to which admitted, registration number, and home county were also recorded on the cards. Similar punch cards in the main record room, accessible by registration number, were already available carrying complete information regarding clinical diagnosis, type of treatment, and disposition of the case. Roentgen-Ray Department records were available in similar form permitting correlation between survey film diagnosis and any subse-

TABLE I

Classification of diagnoses made from survey films:
A. Frank negative admission roentgenogram.
B. Positive admission roentgenogram, which may or may not be clinically significant.
1. Anomalies of ribs.
2. Other bony change, ribs or spine.
3. Abnormal aorta.
4. Pleural changes: apex, axilla, diaphragm, costophrenic angle.
5. Calcification: pleura, lymph nodes, parenchyma.
C. Positive admission roentgenogram, clinically significant.
1. Abnormality, thyroid or mediastinum.
2. Abnormal cardiac size or shape.
3. Non-tuberculous pulmonary disease.
4. Pleural effusion.
5. Intrathoracic glandular tuberculosis.
6. Parenchymal tuberculosis.

quent roentgenologic opinions which had been rendered. The total expense of the test was borne by the Department of Roentgenology as an investigative project. Patients were submitted to subsequent roentgen examination only at the express desire of the clinic staff and for reasons they deemed sound. Neither the economic limitations nor the medical indications of roentgen-ray examination were disturbed.

RESULTS

During the 11 full working days and three half days of the test period a total of 1,116 newly admitted patients were subjected to chest survey examination. Every person passing through the blood-sampling room was so examined. Persons admitted directly to the hospital as emergency patients were not included. The films in 15 instances were for one reason or another unsatisfactory, leaving a total of 1,101 chest films representing a like number of individuals.

The various situations listed in the diagnostic code employed (table 1) are shown in table 2 grouped under the three main subdivisions: *A*, normal; *B*, changes of questionable importance; and *C*, clinically significant situations.

TABLE II

Service	No. Pts.	Class A	Class B	Class C
Unidentified	1		1	
Obstetrics	14	8	6	
Oral Surgery	28	21	5	2
Urology	33	19	18	6
Neurology	60	41	15	4
Ophthalmology	70	48	18	4
Otology	73	43	22	8
Gynecology	75	54	19	2
Dermatology	83	55	24	4
Bone and Joint	89	63	23	3
Surgery	113	73	24	16
Pediatrics	184	164	15	5
Medicine	278	162	80	36
Total	1101	751 (68.3%)	260 (23.6%)	90 (8.1%)

As was to be expected, the majority of the patients examined showed no roentgen evidence of chest abnormality. Group B, those in which non-significant deviations from the normal were observed, is interesting, but one can scarcely justify wholesale roentgen-ray examination on the basis of such returns. It is with the 8.1 per cent, which showed unequivocal changes usually indicative of significant disease, that our chief interest lies.

These 90 individuals had been filtered out of the entire series as persons harboring thoracic situations of prime medical importance. The yield may at first glance appear small, yet when it is remembered that these 90 patients came to the clinic for all manner of situations, it will be recognized that in many instances the discovery of the chest lesion was often times scarcely to be expected on the basis of symptomatology. As a matter of fact, 50 of these 90 patients were cleared through the clinic without being referred to roentgenology, and in but 15 of that 50 was the chest situation, demonstrated by the survey film, diagnosed on the basis of physical findings. This leaves 35 patients in whom chest changes, presumably clinically significant, were observed in survey roentgenograms upon admission whose later study without roentgen examination failed to reveal intrathoracic disease. Careful review of all available data in this selected group of cases showed that in 10 instances the originally observed abnormalities were perhaps open to some question; that in seven instances the abnormality consisted of cardiac enlargement only, while in four instances the probable clinical significance of the observed changes might well be questioned. This process of elimination left a very significant group of 14 patients, representing 15.5 per cent of the entire " C " group, or 1.5 per cent of the entire test series, which must be considered as diagnostic failures in so far as chest status is concerned. These 14 cases deserve individual consideration. Four of these cases showed evidence of pneumonitis of unspecified character.

Case 1. E. P.; f.; aged 40. Admitted 7–5–35 to Otology.
Survey film: Pneumonic infiltration, right median base.
Clinical diagnosis: Previous thyroidectomy and tracheotomy. Vocal cord palsy.
Discharged 7–17–35.
No re-admission.

Case 2. E. M.; m.; aged 59. Admitted 6–27–35 to Neurology.
Survey film: Pneumonitis, right base.
Clinical diagnosis: 1. Left hemiplegia.
2. Latent lues.
3. Borderline heart size.
4. Arteriosclerosis.
Discharged 6–27–35.
No re-admission.

Case 3. I. M.; f.; aged 55. Admitted 7–12–35 to Dermatology.
Survey film: Pneumonitis.
Clinical diagnosis: Rodent ulcer, recurrence.
Discharged 7–12–35.
No re-admission.

Case 4. S. B.; f.; aged 7. Admitted 7–2–35 to Pediatrics.
Survey film: Pneumonitis, right base.
Clinical diagnosis: 1. Strabismus.
2. Tenia saginata.
Discharged 7–2–35.
No re-admission.

The roentgen-ray findings in all of these represent disease which may yet manifest itself by serious clinical symptoms and may well prove to be of serious importance.

Five of the group presented roentgen signs of tuberculosis:

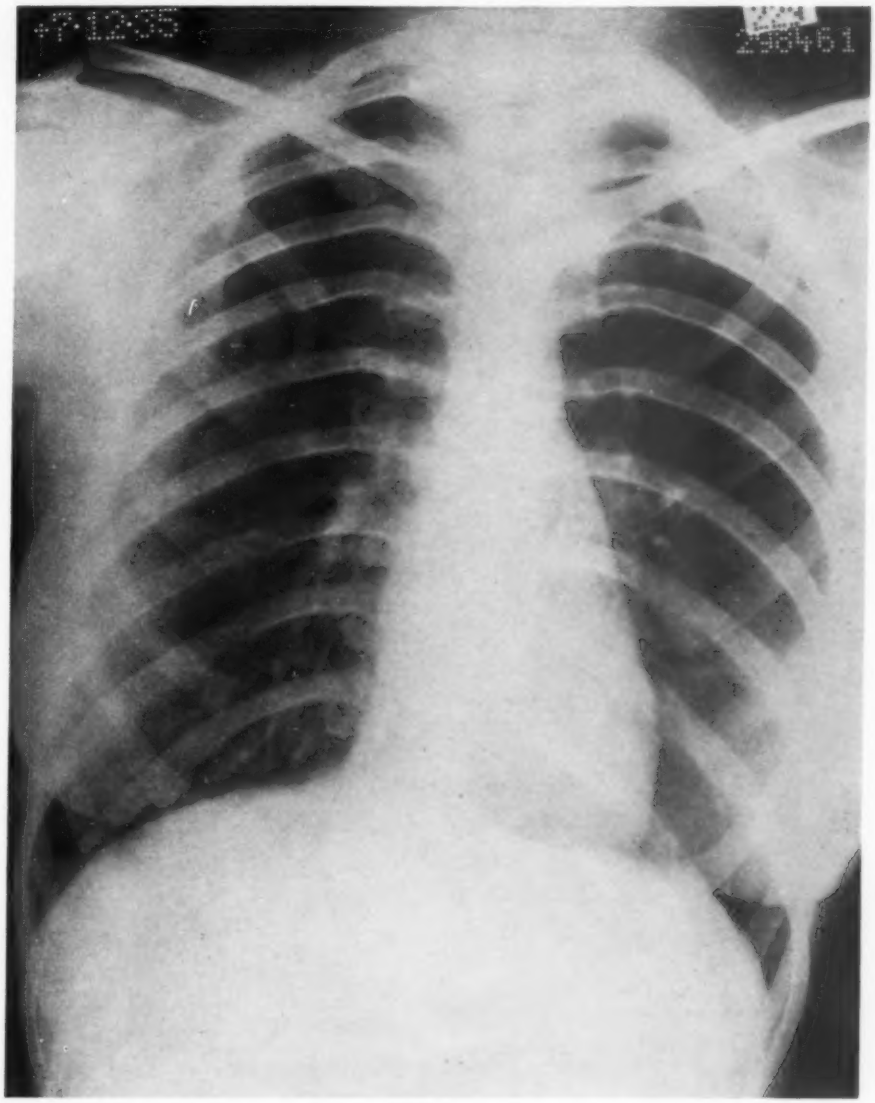


FIG. 1. Minimal pulmonary tuberculosis, left apex.

Case 5. M. T.; f.; aged 17. Admitted 7–12–35 to Orthopedic Surgery.
Survey film: Minimal pulmonary tuberculosis, left apex (figure 1).
Clinical diagnosis: Healed chronic osteomyelitis, right femur.
Discharged 7–12–35 (same day).
No re-admission.

Case 6. J. K.; m.; aged 42. Admitted 7–10–35 to Internal Medicine.
Survey film: Minimal pulmonary tuberculosis.
Clinical diagnosis: Questionable chronic ulcerative colitis.
Discharged 7–16–35.
No re-admission.

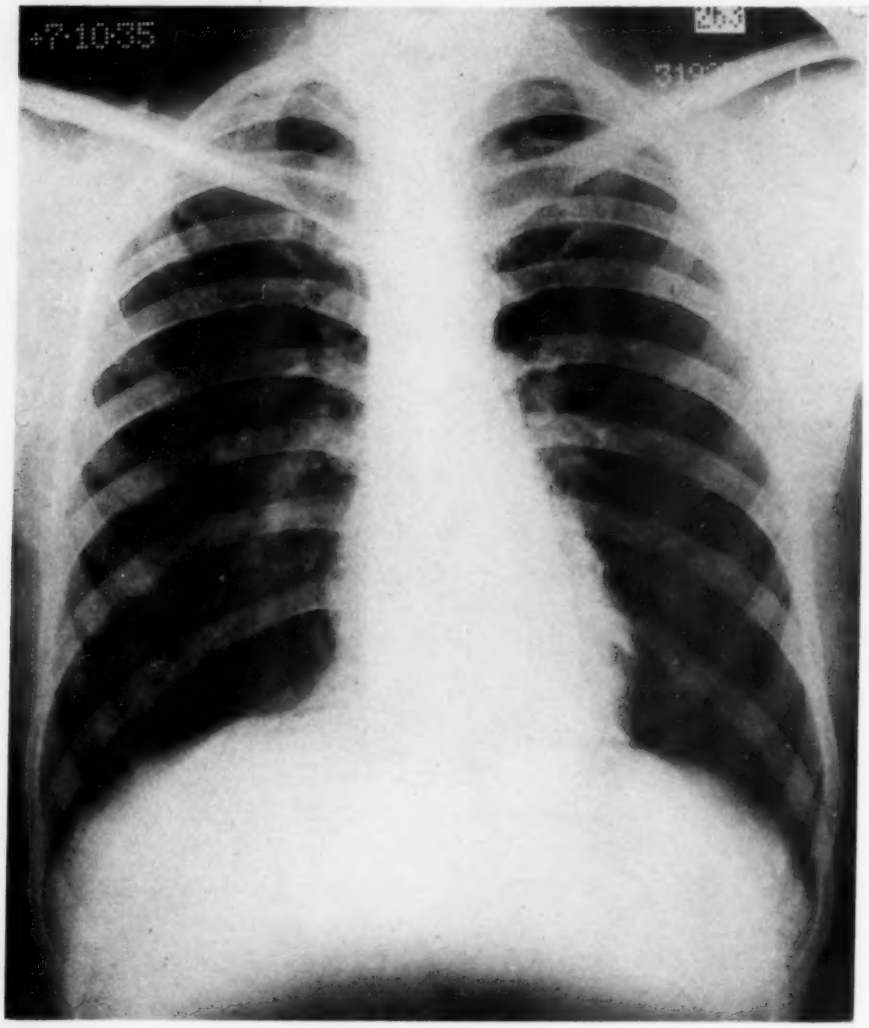


FIG. 2. Minimal pulmonary tuberculosis, right apex.

Case 7. C. M.; m.; aged 26. Admitted 7–10–35 to Oral Surgery.
Survey film: Minimal pulmonary tuberculosis right apex (figure 2).
Clinical diagnosis: Abscessed tooth (tooth extraction).
Discharged 7–10–35 (same day).
No re-admission. Record at University Student Health Service 2–28–36 reveals tuberculosis recognized July 1933. No such information on University Hospital record.

Case 8. G. B.; m.; aged 52. Admitted 7–8–35 to Internal Medicine.
Survey film: Minimal pulmonary tuberculosis.
Clinical diagnosis: Gastritis.
Discharged 7–10–35.
No re-admission.

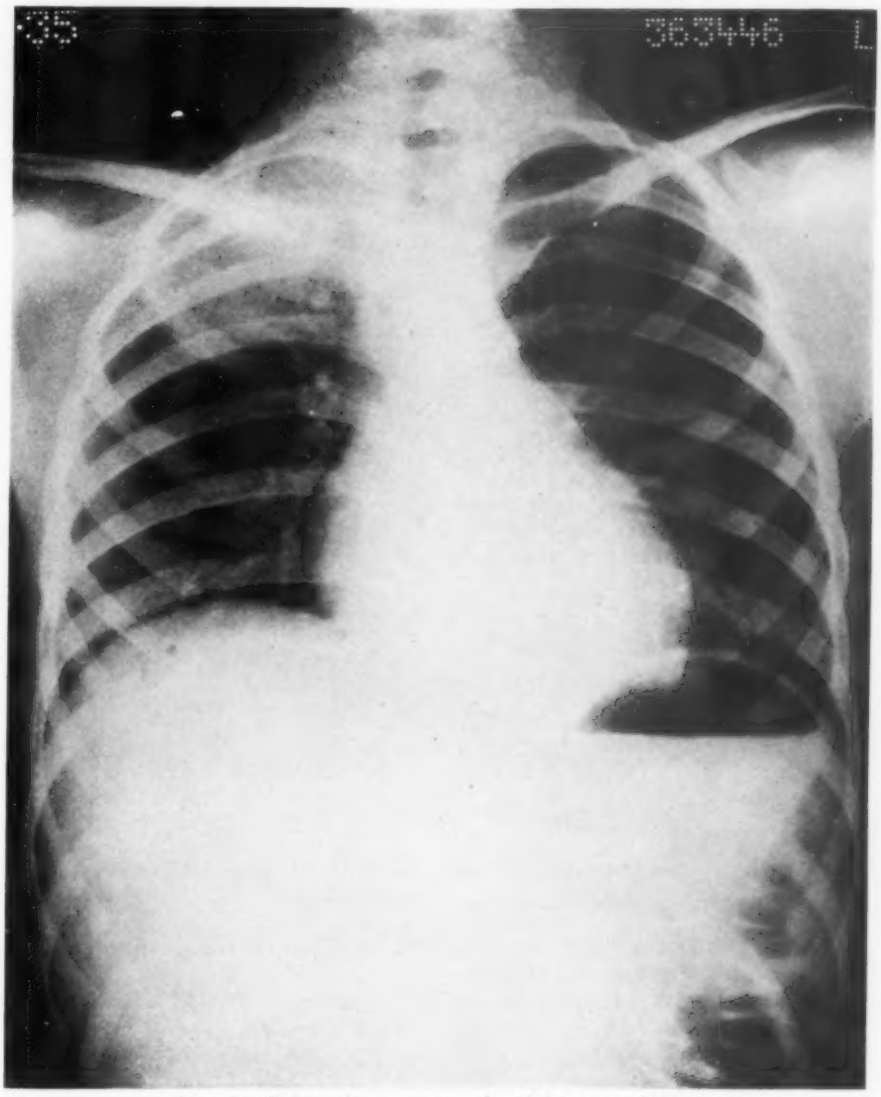


FIG. 3. Tuberculous pneumonia, right upper lobe.

Case 9. A. M.; f.; aged 12. Admitted 7–2–35 to Pediatrics.
Survey film: Tuberculous pneumonia, right upper lobe (figure 3).
Clinical diagnosis: Septic tonsils and adenoids.
Tonsillectomy.
Adenoidectomy.
Biopsy: Negative for tuberculosis of tonsils.
Discharged 7–9–35.
No re-admission.

FIG. 4. Substernal thyroid enlargement and metastatic pulmonary lesion, right apex.

In all of these cases, tuberculosis if recognized would surely have been subject to careful clinical evaluation and treatment.

Case 10. O. D.; m.; aged 19. Admitted 7–1–35 to Orthopedic Surgery.
Survey film: Apparent dextro-cardia.
Clinical diagnosis: Idiopathic scoliosis.
Discharged 8–5–35.
Re-admission.

Without further study the exact cardiac status can scarcely be determined from the single exposure.

Four cases showed evidence of neoplastic metastasis to the lung:

Case 11. F. D.; m.; aged 68. Admitted 7–1–35 to Neurology.
Survey film: 1. Enlarged thyroid.
2. Metastatic pulmonary lesion, right apex (figure 4).
Clinical diagnosis: 1. Cerebral arteriosclerosis—paranoia.
2. Arteriosclerotic heart disease.
Discharged 7–3–35.
No re-admission.

FIG. 5. Metastatic pulmonary lesions.

Case 12. R. H.; m.; aged 35. Admitted 7–2–35 to Otolaryngology.
Survey film: Metastatic pulmonary lesions (figure 5).
Clinical diagnosis: Tubo-tympanitis.
Discharged 7–2–35.
No re-admission.

Case 13. M. G.; f.; aged 65. Admitted 6–27–35 to Gynecology.
Survey film: Multiple neoplastic metastases to lungs (figure 6).
Clinical diagnosis: Undifferentiated medullary carcinoma, uterus.
Roentgen therapy 7–5–35 to 7–9–35; 650 r, 200 KV, to each of four pelvic ports.
Clinical note 8–2–35—" Patient failing "—no further treatment advised.
Death 8–11–35. No autopsy.

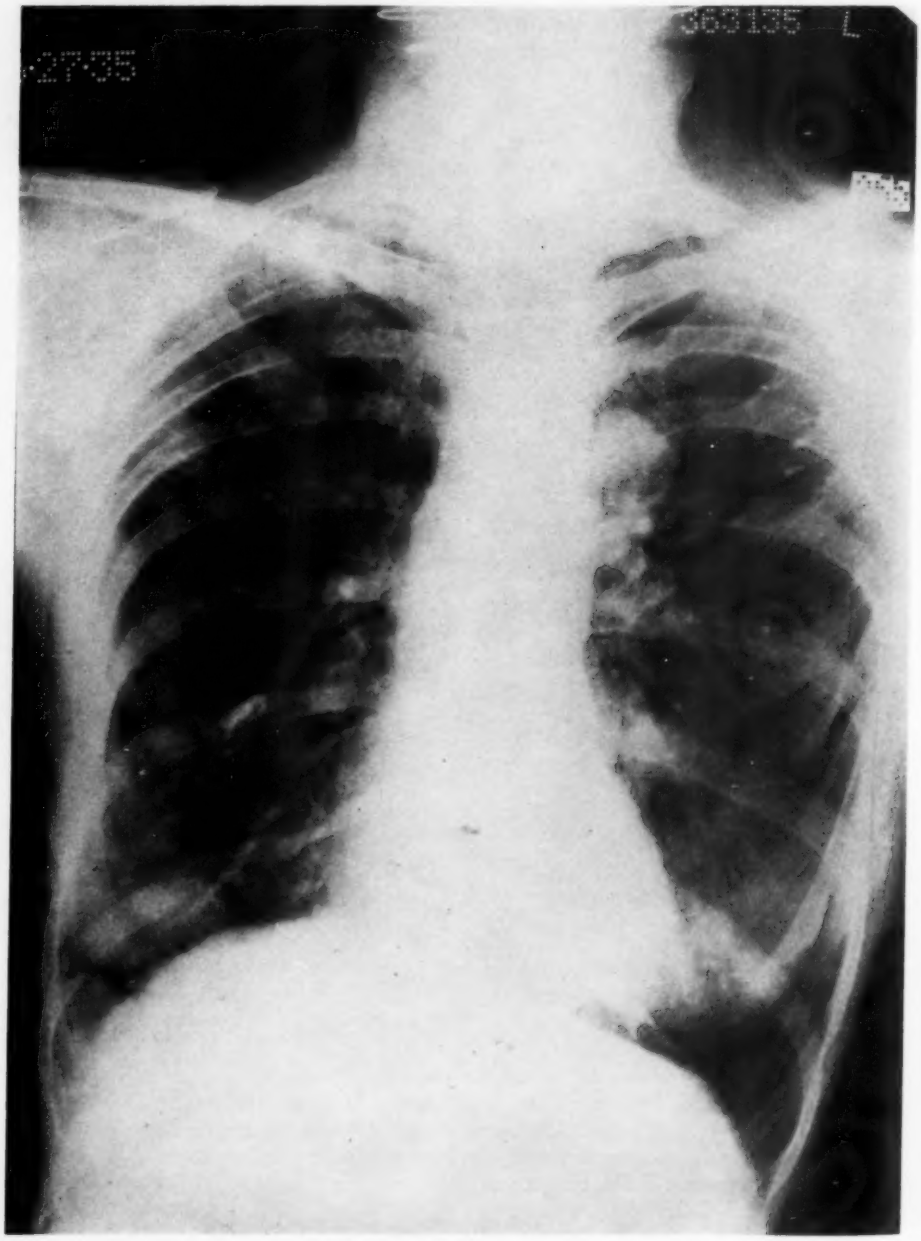


FIG. 6. Multiple neoplastic metastases to lungs.

Case 14. R. W.; m.; aged 67. Admitted 7–1–35 to Urology.
Survey film: Discrete pulmonary lesion. Neoplastic metastasis or primary tuberculous lesion.
Clinical diagnosis: Chronic prostatitis and epididymitis.
Discharged 7–1–35.
No re-admission.
(Unquestionably the handling of these patients would have been altered in the light of positive knowledge of metastasis.)

These 14 instances of overlooked intra-thoracic lesion taken from the total admissions of 14 successive days indicate that we may expect one such oversight as a daily occurrence in spite of the care with which patients are examined. The correction of this situation is of importance not alone to the individual patient in terms of future well-being, but also to the institution and its staff in protecting its reputation for diagnostic accuracy. If insurance against daily errors in diagnosis can be purchased without excessive cost neither physician nor patient can afford to be without its protection.

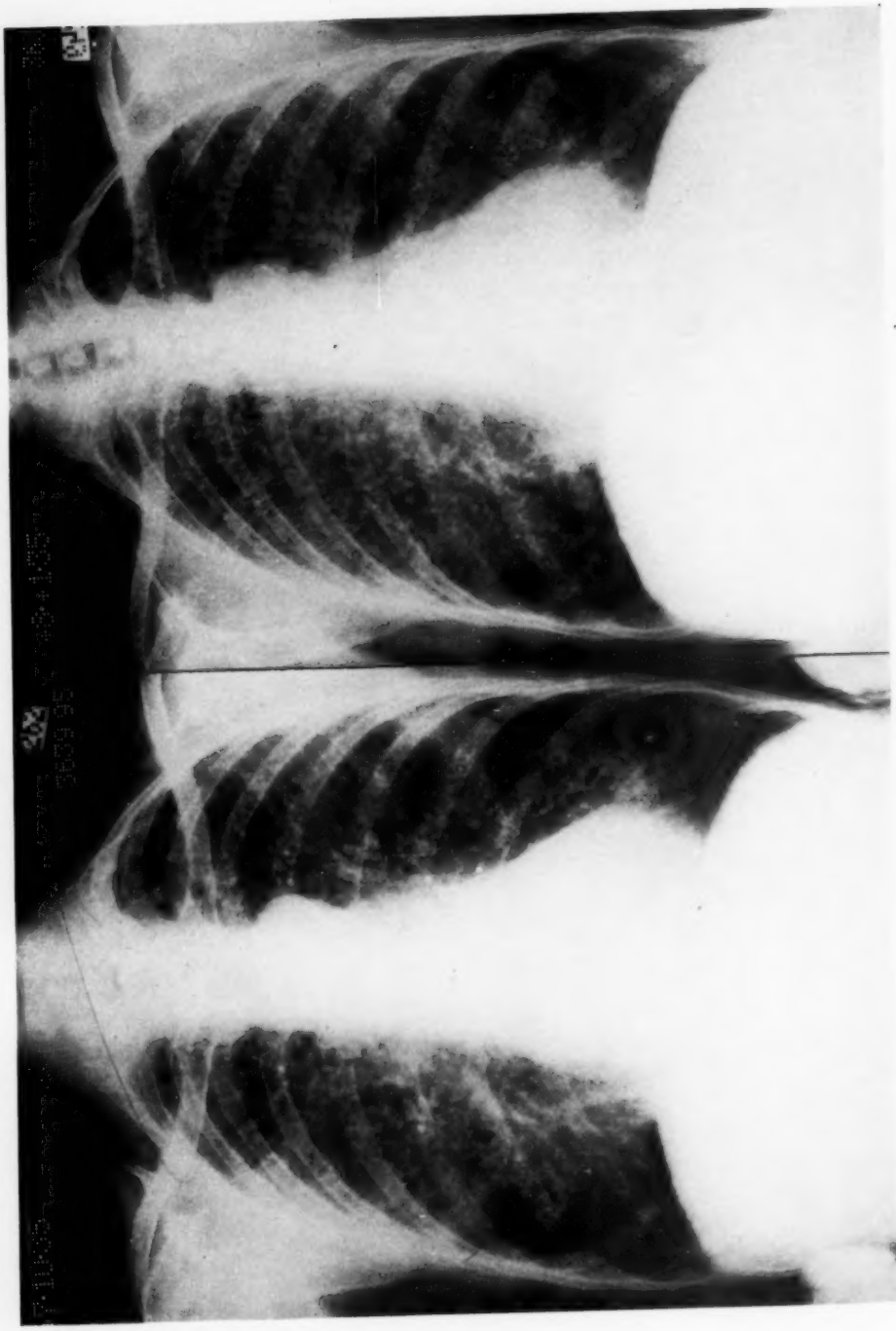
Considering the 40 cases of the "C" group in which accurate diagnosis was later achieved through roentgen information derived from examinations conducted at the request of the clinical staff, one finds that in several instances costly time was lost which would have been saved had the reports of the survey films been made immediately available. This delay amounted to only two days in 29 instances, while in 11 cases 4 to 90 days elapsed before diagnosis was made from roentgen evidence. The average time loss per patient for this group of 40 people was 6.75 days, representing a very real though unnecessary financial load.

Four cases in particular from this group deserve specific mention.

1. R. H.; f. Admitted 7–2–35 to Gynecology.
Survey film: Minimal pulmonary tuberculosis.
Clinical diagnosis: Chronic pelvic inflammation. No response to conservative treatment.
Roentgen-ray consultation, 8–15–35: Minimal pulmonary tuberculosis.
(Still under treatment 3–1–36.)
It is true that the course of treatment was not altered in this case.

2. A. T.; f.; aged 65. Admitted 7–10–35 to Dermatology.
Survey film: Disseminated pulmonary tuberculosis (figure 7).
Clinical diagnosis: Pyogenic ulcer of scalp.
Roentgen examination of skull: Luetic osteitis suggested.
Roentgen-ray consultation, chest, 8–1–35: Disseminated pulmonary tuberculosis.
Death 9–1–35.
Autopsy 9–2–35: Miliary tuberculosis lungs, spleen, liver, peritoneum, and left kidney. Tuberculosis of scalp and skull.
The generalized nature of the disease was unsuspected for 22 days.

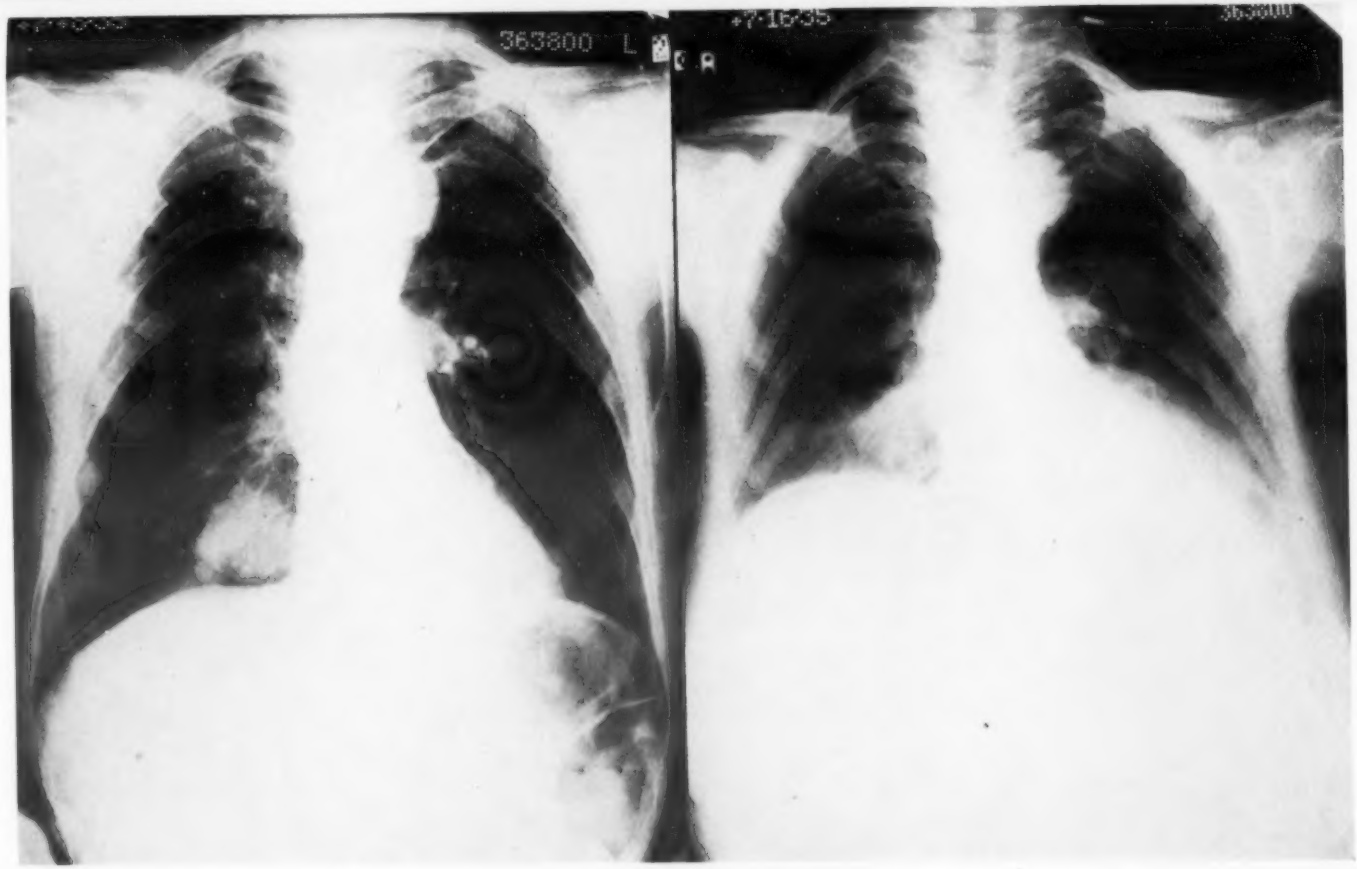
3. M. S.; f.; aged 60. Admitted 7–8–35 to Medicine.
Survey film: Neoplastic metastases right base (figure 8).
Clinical diagnosis: Carcinoma of colon.
Transferred to Surgery: Cecostomy, 7–10–35.



a *b*

FIG. 7. Disseminated pulmonary tuberculosis.

FIG. 7. Disseminated pulmonary tuberculosis.

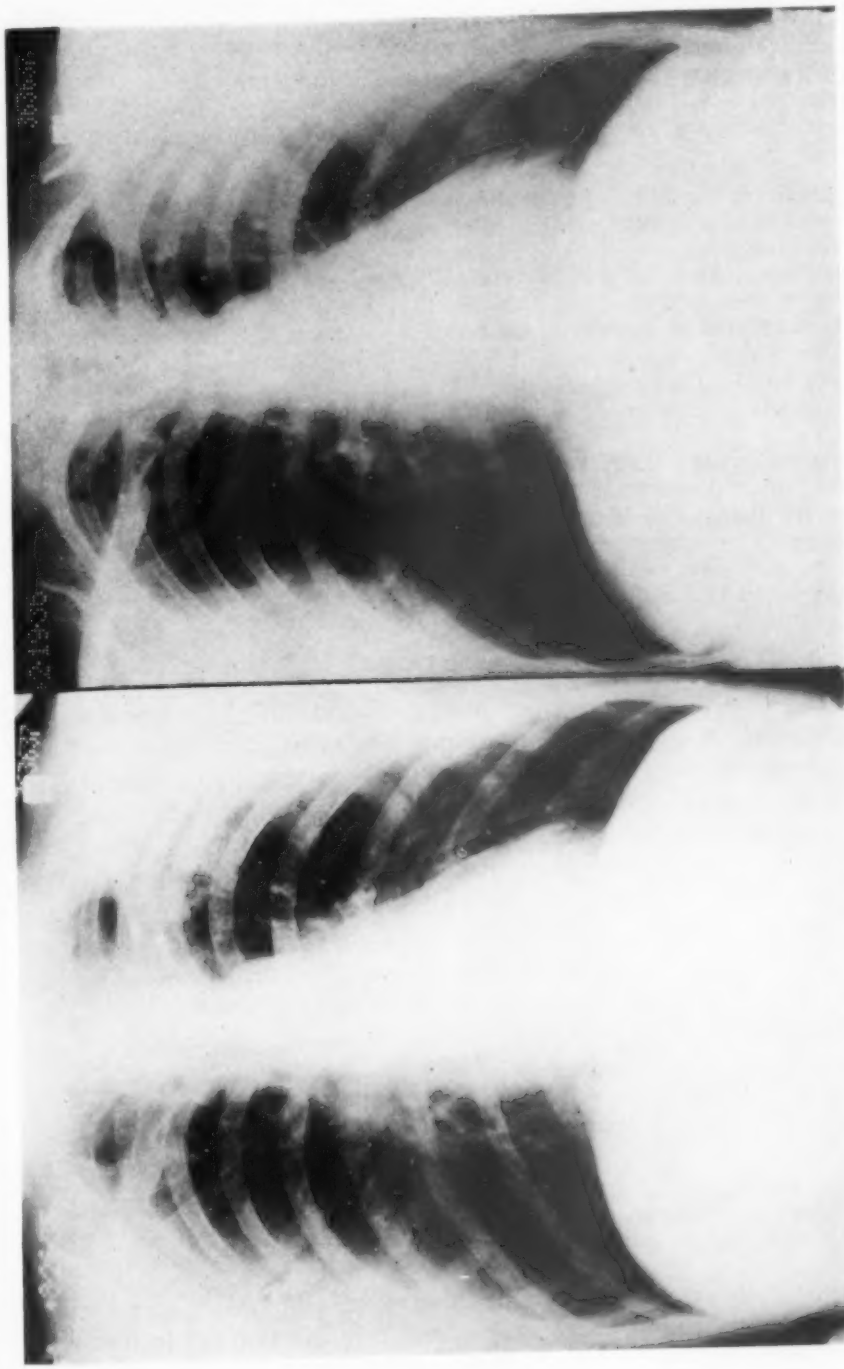


a *b*

FIG. 8. (*a*) Neoplastic metastases, right base. (*b*) Bedside film reported as postoperative pneumonia (respiratory movement resulted in blurring of sharply defined border of lesion).

a *b*

FIG. 9. (*a*) Large metastatic lesion, left upper lobe. (Admission survey film.) (*b*) Same case examined on direct refer 11 days later.



a *b*

FIG. 10. (*a*) Reduction in size of metastatic lesion following roentgen therapy. (*b*) Continued growth of metastatic lesion despite further irradiation.

Roentgen-ray consultation (7–16–35 and 7–18–35) bedside chest examination: Postoperative pneumonia (respiratory movement resulted in blurring of sharply defined border of lesion).

Biopsy via sigmoidoscope 7–27–35: Adenocarcinoma.

Discharged 8–9–35.

Nineteen days earlier the nature and prognosis of this case could have been determined.

4. M. N.; m.; aged 29. Admitted 7–5–35 to Genito-urinary Surgery.

Survey film: Large metastatic lesion left upper lobe (figure 9 *a*).

Clinical diagnosis: Teratoma of testis.

Roentgen-ray consultation 7–16–35: Neoplastic metastasis, left lung (figure 9 *b*).

Roentgen therapy, 7–16–35 to 7–26–35; 1500 *r*, 200 KV, to scrotum; 600 *r*, 200 KV, to each of 10 chest and pelvic ports.

Surgery 8–6–35: Removal of testicle.

Biopsy 8–6–35: Chorioepithelioma.

Roentgen-ray consultation, 8–6–35: Marked reduction in size of chest lesion (figure 10 *a*).

Roentgen therapy 8–28–35 to 9–10–35: 400 *r*, 200 KV, to each of 10 ports.

Roentgen-ray consultation, 1–3–36: Chest lesion enlarging.

Roentgen therapy 1–7–36 to 1–8–36: 600 *r*, 200 KV, to each of 2 chest ports.

Roentgen-ray consultation, 2–19–36: Further increase in size of chest lesion.

A delay of 11 days awaiting result of Ascheim-Zondek test before metastasis was recognized and radiation therapy instituted.

Cost of Survey

Looking into the all important matter of costs of the venture several very interesting facts have come to light. The actual material cost of producing single exposure chest roentgenograms on transparent film by the routine survey plan already outlined is surprisingly low even when one takes into account all items fairly chargeable against the project.

Table III

Material or Non-Professional Cost of Survey

Capital cost	$50.00*
40 gallons of developer @ 45¢	18.00
40 gallons of fixing solution @ 20¢	8.00
Technician 14 days @ 35¢ per hour	39.20
Ward-helper 14 days @ 33¢ per hour	36.96
Dark room labor 4 hours daily, 14 days @ 50¢ per hour	28.00
Stenographic service 32.5 hours @ 50¢ per hour	16.25
1116 14 by 17 films	558.89
	$755.30

* *Note.* This figure represents a total capital investment for chest radiographic apparatus $5000.00 plus $1000.00 for necessary building alterations with interest at 6 per cent amortized over a five year period which is customary in this institution.

It is our intention, if and when the chest survey plan becomes a permanent feature in this institution, to use transparent celluloid film cut to the special size of 13 by 14 inches. This will mean narrowing the film by one inch and shortening the film by three inches which in the majority of cases will permit

inclusion of the entire thorax. For unusually large patients, 14 by 17 films can still be used, and conversely for small children 11 by 14 or even smaller films can be used. Since film costs vary directly with film area this will permit a still further reduction in the material cost of this type of examination. In fact, had the 13 by 14 size been used in this particular test the saving would have amounted to $168.29. This additional saving will more than cover the customary 25 per cent charged against all budget expenditures in this institution for general administration overhead.

At this point it should be emphasized that over and above the preparation of satisfactory roentgenograms at material costs such as those already enumerated, the examination of such films by physicians trained in their interpretation is all-important if a survey of this sort is to have any medical value whatever. It goes without saying that this medical service entails further expense which can by no means be overlooked. By well established precedent throughout all branches of medicine the right to establish a suitable fee for his own personal services has long been reserved to the physician himself. It is not the intention of this communication to suggest what a proper fee for this medical service should be, but rather to point out that established roentgen laboratories, whether privately owned or operated by hospitals or clinics, can render an exceedingly valuable service to referring physicians at a cost which need not be prohibitive. It will be remembered that the plan calls for a simple survey of the chest of *all* new admissions in order to quickly uncover unsuspected manifestations of disease within the thorax, to provide a record of that patient's chest for future reference and to direct both the roentgenologist and the referring physician in the matter of requesting and carrying out further, more detailed studies in those cases where further study seems advisable. It must not be inferred that present fees for individual stereoscopic examination of the chest or other special procedures are necessarily exorbitant. The reporting of survey films by mere indication as to whether the chest appears to be barren of pathological changes, shows evidence of changes which though interesting may not be significant, or shows definite evidence of abnormality requiring further study, is not time consuming and, if done in quantity, is not costly from the material viewpoint nor need it be costly from the professional viewpoint.

Summary

To test the theory that it would be profitable to subject all persons presenting themselves for physical examination and treatment to a preliminary roentgenographic survey of the chest, this sort of examination was conducted on all patients registering at the University Hospital for a period of 14 successive clinic days. At the outset it was postulated that five conditions must be met if the plan were to be considered practicable. The first of these conditions, "increased diagnostic accuracy," was adequately met by the final results for a conservative estimate shows that in the group of

patients so studied 14 were found to present significant, if not alarming, chest situations which were not discovered by other means.

The demand that the survey plan must demonstrate the ability to "increase diagnostic speed" was well shown by the fact that patients with significant chest changes, ultimately satisfactorily diagnosed, could have had these diagnoses pronounced on the average of 6.75 days sooner.

It was postulated that the plan should constitute "no added financial burden to patients," that the aggregate roentgen-ray cost to the group of patients so examined did not exceed the amount paid by those few who by one method of selection or another might be sent for roentgenological examination of the chest in the ordinary course of events. Actually, of the total group surveyed numbering 1116 individuals, 164 patients were referred in for chest examination, the results of the admission survey having been withheld. These individuals actually paid in the aggregate $99.00 more than the material cost of surveying the entire group. It is further true that the total survey cost did not include professional fee for interpretation. If one is willing to offset this additional cost to the patient group by the indeterminate saving, certainly to be affected by the reduction in time of complete examination set forth in the preceding paragraph, it may be assumed that no additional cost would have been imposed upon the patient group.

It is impossible to determine accurately the extent of any possible loss in revenue in the Roentgen-Ray Department which the fourth postulate insisted must not occur. It seems logical to assume that the 50 patients shown to have definite pathological changes in the chest, who were not subsequently subjected to roentgen examination at the request of the examining physician, would have been studied more thoroughly had the survey findings been known. Though the Department of Roentgenology would undoubtedly lose certain chest examinations done more or less on suspicion by the referring physician, it would at the same time gain more interesting and more extensive work as the result of the discovery of unsuspected chest lesions in the survey process.

The fifth and last condition to be met; namely, that roentgenological service presumably valuable might be extended to all patients by spreading costs has undoubtedly been satisfactorily shown to be true. Many of the benefits to be derived from a survey of this sort are not at first glance recognizable. Months, even years after the patient's original admission subsequently developing chest lesions may be compared in so far as their roentgen appearance is concerned with that same chest as it appeared on the date of first admission.

Conclusions

1. The methodical practice of submitting all patients presenting themselves to a hospital or clinic for physical examination to routine roentgenographic examination of the chest can be accomplished expeditiously and without great inconvenience to the patient.

2. Roentgenographic chest survey of all hospital and clinic admissions assists the examining physician in quickly determining which patients may profitably be subjected to more searching examination by the roentgen method.

3. Routine chest survey may be expected to disclose alarming chest changes in approximately 8 per cent of patients presenting themselves to a general hospital or clinic.

4. Significant chest disease unrecognizable by other methods and often totally unexpected on the basis of chief complaint and history may be expected in something over 1 per cent of large, diversified patient groups.

5. Roentgenographic chest survey offers a means of increasing the speed with which obscure chest situations may be accurately diagnosed.

6. The cost of offering this one type of roentgenographic service to all patients need not constitute an unwarranted financial burden upon patients.

CHRONIC ARTHRITIS, A GENERAL DISEASE REQUIRING INDIVIDUALIZED TREATMENT *

By Ernest E. Irons, F.A.C.P., *Chicago, Illinois*

Hundreds of discussions and scores of books have been written about arthritis—and still they come, largely because this condition occasions more disability than any other disease in temperate climates, and its care presents a greater multitude of difficulties. In presuming to bring to you so age-worn a subject, I plead as excuse the request of your President, and the fact, expressed in my title, that in recent years there has come a great change in the general conception of the relation of disease of the joints to disease of the rest of the body. This altered viewpoint makes easier the understanding of the variable course and symptomatology of arthritis, and facilitates the formulation of a program of treatment suited to each patient. I can offer little that is new, but perhaps may present old observations in a relationship which will be serviceable in planning treatment.

Before passing to the problems of chronic arthritis it is of interest to recall that much acute arthritis is clearly related to infections, and occurs as a part of the general infectious process. Frequently the causative organism such as gonococcus, streptococcus or pneumococcus is demonstrable in cultures from the infected joints. The number of joints involved, however, is remarkably small when considered in relation to the number of times that bacteria must reach joint structures in the course of the demonstrated bacteremias of infectious diseases. Furthermore, the infected joints usually heal under appropriate treatment and rest, without residual impairment of function. We may conclude that the cartilage and other joint tissues of normal persons are fairly resistant to infectious insults.

This suggests that when joints fail to heal, and the arthritis passes into more chronic forms, factors other than the initial infection, such as inferior cartilage, impaired blood supply and nutrition, may be concerned in the disease.

Causes other than infection such as serum disease, hemorrhagic diseases, as well as trauma, may also initiate acute arthritis. The parallelism noted between the acute arthritic phenomena of serum disease and the exacerbations of arthritis in rheumatic fever can be readily extended to some of the acute exacerbations of chronic arthritis which follow acute respiratory infections.

The concept of chronic arthritis as a general disease, rather than one of the joints alone, is steadily gaining ground. It is generally conceded that there are many initiating and contributing causes of chronic arthritis. These include infection, trauma, the wear and tear of use, heredity, dis-

* Presented at the Detroit meeting of the American College of Physicians, March 2, 1936.

turbances of vascular supply or of general and local nutrition, metabolic and glandular dysfunction and the degenerative changes of advancing age. Various combinations of these causes and conditions in individual patients result in varying clinical pictures, whose common factor is involvement of joints and structures attached to the bony skeleton. No one single cause or condition is common to all cases of arthritis.

Many classifications of chronic arthritis have been suggested, but as so often happens the simplest seems the best, and the division of chronic arthritis into atrophic (rheumatoid) and hypertrophic (osteo-) arthritis, suggested by Garrod in 1890, and by others later, has been adopted by the American Committee. The British Committee suggests a classification, similar but somewhat more elaborate.

Atrophic (proliferative, rheumatoid) arthritis occurs in the younger age groups, often in women, and is characterized by multiple joint involvement with fusiform appearance of joints of fingers, often ulnar deflection, and later ankylosis. The onset is either insidious or acute, and evidence of initial and often of continuing infection is frequent. In many patients constitutional effects with slight fever, anemia, and poor nutrition are marked.

Hypertrophic arthritis begins on the average somewhat later, or beyond middle life, in persons often well-nourished, and causes disability from slight to severe crippling. It is usually polyarticular but may be monarticular. Lipping of joints, and hyperostoses are frequent; ankylosis is rare. Fibrous thickenings, Heberden's nodes with later bony hyperplasia at the terminal joints of the fingers are common. The effects of the trauma of work are often noted in the hands and spine of the laborer. Evidences of infection are much less frequent than in the atrophic form and when discovered, their removal influences but little the course of the arthritis. Arthrosis, which has been suggested to replace the term arthritis of this type, has at least the virtue of being less committed to the inflammatory concept.

Certain difficulties are met with, however, in accepting the dictum that the two types are etiologically and clinically distinct diseases in the same sense that lobar pneumonia and typhoid fever are from the beginning, by reason of their etiology, different diseases.

Now and then joints in the same patient show in one the pathologic anatomy commonly found in atrophic arthritis and in another the pathologic changes of hypertrophic arthritis. While evidences of infection predominate in atrophic arthritis and are usually minimal in hypertrophic arthritis, there are exceptions in which acute inflammatory processes occur in the hypertrophic form. The Heberden nodes, frequently found in chronic hypertrophic arthritis, may at times become acutely tender, red, and swollen following acute (such as respiratory) infections. Trauma of work, a large factor in hypertrophic arthritis, also appears in evidence in atrophic arthritis in which the right hand in a right handed person shows more extensive change than the left.

The location of the affected joint and the degree of its exposure to the trauma of weight bearing have been shown to influence the type of arthritis which develops. The effect of heredity seems as clear in atrophic arthritis occurring in grandmother, mother and daughter as in the family incidence of early hypertension. Racial, familial and individual peculiarities in connective tissue response to injury, as illustrated by the variable formation of keloid in surgical scars, and the varying rapidity and extent of callus formation after fractures indicate the wide range of individual tissue response to trauma. The same factors undoubtedly influence the healing of tissues of joints.

Is it not possible that the disease process in chronic arthritis assumes this or that course with the production of one or another type of arthritis by reason of the kind, age and resistance of tissues of the patient whose joints have suffered an initial insult? It may even be argued that the same insult which initiates in one person an atrophic arthritis, might, if received by a person whose tissues were less vulnerable, have caused no more than a temporary disability. In this connection, consider the variety of types of arthritis which may follow gonococcal infection, from an acute temporary and quickly healing arthritis, to the chronic forms, indistinguishable from " atrophic arthritis " or again from spondylitis ankylopoietica of the British classification.

The predominance of infection in atrophic arthritis as compared to hypertrophic arthritis is evident, but the cause for this predominance may well lie in the poor resistance to infection of the patients' tissues in general, including those of the joints, which also in these cases are less well able to withstand injury and heal than are those of persons with a better heredity.

In this sense we may regard the person whose general resistance to infection is below the normal, and whose cartilage and joint tissues are by reason of heredity less able to withstand insults and to heal than are those of normal persons, as potentially a candidate for atrophic arthritis. In such a person, further lowering of resistance to infection, malnutrition, overwork, extreme nervous strain, as well as severe infections, especially those of the respiratory tract, become etiologic factors in the atrophic arthritis which follows. The arthritis which gives the clinical name to the condition is thus only one expression of the more fundamental general disease.

It is generally agreed that the division of chronic arthritis into two great groups, the atrophic (rheumatoid) and hypertrophic (osteo-) arthritis is extremely serviceable. One of the chief values of this classification rests on the fact that it takes into consideration the previous reactions of the tissues of the patient and so prophetically indicates the kind of changes he is likely to suffer in the future, and, therefore, the measures which should be taken to meet and modify the disability which threatens him.

Borderline cases, and those in which both types are found in the same patient, are accounted for by unusual combinations of causes including vary-

ing exposure to trauma, and the peculiar tissue reactions of the individual patient.

With this multiplicity of continuing causes of chronic arthritis in mind, the original initiating cause, not infrequently undeterminable, becomes less important, and the care of the present problems of the patient moves to the fore.

Again, we may ask, does the presence or absence of infection determine the course and type of the arthritis, or is infection present (either active, or apparently not participating in the progress of the disease) by reason of decreased general body resistance to infection, and not because of the presence of arthritis? If the latter, we may then conceive of atrophic arthritis as occurring in persons whose cartilage and joint structures heal less readily when injured than in the usual normal person, and whose resistance to infection is also below the normal. When such a person suffers from an infection his joints are less likely to escape, and once involved, healing is incomplete and the process becomes a progressive one. He is likely to suffer from recurrent infections especially streptococcal, with exacerbations of joint disease, and studies of his blood will show the evidences of infection.

The process in the joints, which gives the name of arthritis to the illness, is subordinate to the more fundamental basic constitution of the patient, in respect to his general resistance to infection, and to the ability of his joint tissues to heal or to resist varying degrees of trauma. Again the emphasis falls on the general features of disease in the body rather than on that in the joints alone. In the established case of hypertrophic arthritis, infection seems to play but a minor part, nutrition suffers little, there are degenerative changes in cartilage and much of the disability results from marginal ossification, and mechanical interference with joint motion.

Treatment

Clinical experience and methods of treatment of chronic arthritis have progressed through the study of the effects of treatment of groups of patients by one or another method, such as the search for and removal of infections, the giving of this or that drug, attempts at immunization by vaccines, the use of special diets or the employment of physical therapy. These surveys have required enormous expenditure of effort, and an industry that commands admiration. Some of these studies have been well controlled and have taken into consideration the natural history of arthritis and its well recognized tendency to spontaneous remissions. Others have consisted of uncritical observation of many patients for short periods, and are of little or no value.

Some patients have been benefited by each of the remedies exhibited but, as might be anticipated, no one remedy has proved to be curative in a large proportion of groups of patients so selected.

No two patients present the same combination of symptoms, nor are

their problems to be met in exactly the same manner. Different combinations of causes may result in arthritis of essentially the same type, although certain causes undoubtedly tend to be associated with one or the other type. The type of arthritis which will develop depends on the age, nutrition and kind of tissues of the patient.

For purposes of a general survey and classification of arthritis, the study of patients in large groups is necessary, but for purposes of treatment and cure the unit of study is the individual patient. In chronic arthritis, as in the solution of current economic problems in medicine, methods of mass production are bound to fail.

There are certain general and special measures from which can be selected those applicable to each patient. Rest for the patient as well as for his joints heads the list. In many cases this means rest in bed. Removal of causes of worry and apprehension in so far as this can be accomplished in these times of unrest is as essential as physical repose. Elimination of infection is of first importance in many, and will contribute to the improvement of still other patients.

A well-balanced diet, including milk, eggs, meat, fruit and vegetables, affording full caloric requirement, with ample protein and fat, is important especially in atrophic arthritis. In the obese, reduction of weight will give relative relief from trauma to weight bearing joints. Reduction of carbohydrates may at times decrease local swelling and distress of joints. A diet excessively high in sugar and starches, frequently adopted by patients invalided with arthritis, is undesirable also because it is likely to be deficient in proteins, fat, and vitamins and contains insufficient residue to provide for efficient elimination. An abundant fluid intake will promote elimination by the kidneys and bowel.

Most of the drugs specially devised for the treatment of arthritis have not justified the claims made for them. In general the trend is away from excessive drug therapy in arthritis. Preparations of the salicylic group are useful for their analgesic action. Iron and other antianemic drugs in combination with diet are of great value in combating anemia. Thyroid deficiency, frequently present in chronic arthritis, is met with appropriate doses of thyroid extract. Vaccines as a routine treatment are as ineffective as are certain of the widely heralded drugs. There are, no doubt, many instances in which vaccines have been helpful, but more often they have been used as a sort of occupational therapy by patient and physician, sometimes to the exclusion of more effective agencies.

In addition to measures taken to remedy general anemia and malnutrition of the patient, local treatment to improve nutrition and circulation in the joints is required. Heat, dry and with moist packs, combined with gentle massage increases local blood supply. The degree of active and passive motion to be employed is to be determined in each case, with the necessity of gentleness always in mind. For these purposes, simple appliances and those improvised in the home are desirable. In the past year we have been

treating the cold clammy extremities of atrophic arthritis with negative pressure by means of the Pavaex machine. The skin temperature is increased, and in the small group of selected patients so treated the joints have improved.

Chronic arthritis, especially in its advanced stages, requires skilled orthopedic care. Much may be accomplished in correction of deformities and improvement of posture of the arthritic. More important still is treatment earlier in the disease, to prevent deformities and contractures. If ankylosis is unavoidable, positions of joints most serviceable to the patient should be secured.

In spite of the present popularity of vitamins, it would seem that much of the reputed necessity for vitamins may be obviated by moderate attention to the maintenance of a balanced diet including the conventional articles of milk, fresh fruits and vegetables, eggs and meat. In so far as there is probability of an unavoidably incomplete diet or lack of sunlight, the vitamin deficiency may be supplied in form and amount necessary for the general welfare of the body. There is still some doubt as to the wisdom of supplying this or that vitamin in large doses for the cure of disease of the joints. Neither is an immediate favorable effect on the joints clearly proved, nor have the more remote, and possible unfavorable effects of massive doses of vitamin-containing substances on human tissues been determined.

Gout is not so rare as some have thought, and may occur alone or in combination with either of the two great types of chronic arthritis. Preparations of colchicum, and appropriate modification of diet are as effective as ever in gout.

Osteochondritis or epiphysitis of the spine originating in rapidly growing children with characteristic lesions involving the vertebral bodies may cause early pain, disability and bone deformity, and in later life contribute to osteoarthritis. The recognition of these lesions by means of the history and by the roentgen-ray will obviate a fruitless search for local infections and suggest necessary rest and support for the painful backs of these youngsters.

Much can be done for the patient with chronic arthritis. Recognition and treatment of his general defects in nutrition and in resistance to infection, and his individual tissue response to injury, are as important as treatment of his joints. The resultant of causes and tissue responses is recorded in the changes already evident in the joints.

Classification of chronic arthritis into atrophic and hypertrophic types is advantageous and practical. While it may express to a varying extent etiologic factors, it is more important as an indication of the aggregate result of both general and local causes which have been active in each patient, and of the probable subsequent course of the disease.

The patient with arthritis is best treated not as one of a crowd, but individually, with reference to his own special problem of general as well as local disease.

TREATMENT OF PNEUMONIA WITH SERUM CONTAINING TYPE-SPECIFIC, HETEROPHILE, AND NEUTRALIZING ANTIBODIES *

By VERNER B. CALLOMON, M.D., and JOHN UNGAR, JR., M.D.,
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THE value of the conventional antipneumococcus sera, both unconcentrated and concentrated, has been shown to lie for the greater part in their content of type-specific protective antibodies. Unfortunately, their field of usefulness has been restricted chiefly to Type I infections, although there is some evidence of activity in Type II and in Types VII and VIII infections.[1] In Type III and most Group IV infections evidence of any curative value is lacking. For some years immunologic observations have been accumulating which have led to the preparation of an antipneumococcus serum containing additional immune factors.

In 1911 Forssman [2] observed that the injection of guinea pig tissues into the rabbit results in the production of antibodies which not only react with their homologous antigen, but also hemolyze sheep's red blood cells. Because these antibodies react with antigens other than those which produce them, the term heterophile has been applied to both antibody and antigen. It later developed that this type of antigen is present in a variety of animal and bacterial species, while absent in others. Injection of heterophile antigen into animals in whose tissues it is lacking results in the formation of heterophile antibodies. This does not occur when animals whose tissues contain heterophile antigen are so injected. Among the animal species containing heterophile antigen are the guinea pig, cat, dog, mouse, chicken, and horse. Among those containing none are the ox, rat, rabbit, and man.

In 1931 Bailey and Shorb [3] published the results of experiments from which they concluded: That heterophile antigen is present in pneumococci, and in common with heterophile antigen from other sources is capable of inducing the production of heterophile antibodies when injected into the rabbit. These antibodies react with heterologous as well as homologous types of pneumococci. They also reported that serum from human convalescent pneumonia patients shows a definite increase in heterophile antibody titer.

This latter observation has failed of confirmation by Finland, Ruegsegger, and Felton, who recently reported their inability to demonstrate significant increases in heterophile antibody content of serum from human pneumonia cases or from cases immunized against pneumococcal antigen.[4]

Further experiments by Bailey and Shorb [5] were reported in 1933.

* Received for publication December 13, 1935.
From the Section on Respiratory Diseases, Division of Medicine, Allegheny General Hospital.

These bore out their earlier conclusion that pneumococcus heterophile antibodies are not type-specific, and in addition disclosed that the heterophile antibodies in antipneumococcus rabbit serum are partially neutralized by normal horse serum, and to a greater degree by antipneumococcus horse serum. This, of course, demonstrates the presence of natural heterophile antigen in normal horse serum and the increase of heterophile antigen in antipneumococcus horse serum. Furthermore, they found that the addition of various proportions of antipneumococcus rabbit serum to antipneumococcus horse serum enhanced its opsonic power for pneumococci. This opsonic activity seemed to be intimately associated with the heterophile antibody fraction.

In 1930 Jamieson and Powell [6] found that some pneumococcus filtrates contain toxic substances which can be demonstrated and measured by intradermal tests in human beings and certain breeds of rabbits. They were able by subcutaneous injection of horses to produce sera having the property of neutralizing these toxic substances. These sera were not type-specific, but appeared active against filtrates of all types of pneumococci. They also observed that serum from convalescent human pneumonia cases contained such skin test neutralizing substances.

In 1933 Powell, Jamieson, Bailey, and Hyde,[7] realizing that the conventional antipneumococcus horse serum falls short of the ideal because of its content of heterophile antigen and lack of heterophile antibody, carried out experiments with various combinations of antipneumococcus rabbit and antipneumococcus horse serum in the treatment of pneumococcus infections in rabbits. They found that such combinations were much more effective therapeutic agents than either serum used singly.

Laboratory investigation and animal experimentation having given such encouraging leads, a clinical trial of the use of such a preparation in the pneumococcus pneumonias of man seemed indicated. A composite serum has recently been prepared for this purpose. In its preparation horses are immunized by intravenous injections of virulent cultures of Types I, II, III, and IV (Type IV of Group IV of Georgia Cooper) pneumococci, and subcutaneous injections of whole culture toxic vaccine of the same types. When by trial bleedings sufficient type-specific protective potency for Types I and II pneumococci and sufficient neutralizing value has been determined, the serum is drawn, refined, and concentrated. Rabbits are immunized by intravenous injection of the same types of pneumococci. Their serum is tested for heterophile antibody, refined, and concentrated. The horse and rabbit antisera are then mixed in such proportions that the heterophile antigen present in the horse serum is precipitated and filtered out, and a final titer reached of 10,000 conventional mouse protective units each of Types I and II, 100,000 skin test neutralizing units,[6] and 50,000 heterophile antibody units [7] in each therapeutic dose.* In comparing the finished product with

* Description of preparation taken from information received from Eli Lilly and Company, Indianapolis, Ind., whose generosity in supplying the serum used in this study is gratefully acknowledged.

the hitherto available conventional, concentrated sera of the Felton type, it is at once apparent that they are alike in their content of type-specific protective antibodies against Types I and II, but differ in that in the composite serum heterophile antigen has been eliminated and heterophile and neutralizing antibodies have been added.

Experience with the use of this serum in the treatment of a series of cases of pneumococcus pneumonia in Pittsburgh during the season of 1934 to 1935 forms the basis of this report. It was planned arbitrarily to select for this treatment cases of proved pneumococcus pneumonia which came under observation not later than the fourth day of their disease, and which were not obviously complicated. As will appear, a few cases received serum therapy which were later found not to have these qualifications. These latter cases will receive separate consideration. Before instituting serum treatment, in addition to a history, physical examination, blood count, and sputum examination, a roentgen-ray of the chest was taken when possible in order to establish the diagnosis conclusively. Blood cultures were taken at two-day intervals in all cases but one which was treated outside of the hospital. Sputum was regularly typed, but no attempt was made to further differentiate members of Group IV. Following the establishment of the diagnosis, a therapeutic dose of serum was given intravenously at four- to six-hour intervals for approximately 10 doses, or until the fever subsided and showed no tendency to rise again. Prior to giving the serum, intracutaneous and ophthalmic tests were made to avoid dangerous serum reactions. Supplementary treatment consisted only of limitation of diet to liquids including an adequate supply of fruit juice fortified with dextrose, daily enemas as required, and symptomatic medication, such as oxygen and morphine, when indicated. Of 32 cases treated by this method, 24 cases are included in this series as having all the qualifications originally demanded. Brief case outlines follow:

Case Reports

Case 1. J. L. W., male, Indian, aged 42. Admitted November 19, 1934. Lobar pneumonia, right upper lobe. Onset one day prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. Roentgen-ray: confirmatory. Serum treatment instituted on third day of disease 24 hours after admission. Five ampoules of serum given in 40 hours. Death occurred on fifth day of disease. Autopsy: lobar pneumonia with multiple abscesses of lung.

Case 2. J. F., male, white, aged 49. Admitted November 26, 1934. Lobar pneumonia, right hilus. Typical onset one day prior to admission. Sputum: pneumococcus Type I. Blood culture: pneumococcus Type I. Roentgen-ray: confirmatory. Five ampoules serum given within 24 hours after admission. Recovery by rapid lysis.

Case 3. N. S., male, white, aged 68. Typical onset, December 8, 1934. Lobar pneumonia, right lower lobe. Sputum: pneumococcus Group IV in large numbers. Blood culture: not taken. W. B. C., 24,200. Serum started 17 hours after onset. Three ampoules at six hour intervals. Recovery by crisis.

Case 4. J. H., male, white, aged 44. Admitted January 5, 1935. Lobar pneumonia, whole right lung. Onset one day prior to admission. Sputum: pneumococcus

Type I. Blood culture: pneumococcus Type I. W. B. C., 30,650. Roentgen-ray: confirmatory. Eight ampoules of serum given within 48 hours after admission without terminating illness. Type I convalescent whole blood (250 c.c.) given over fifth, sixth, and seventh days of illness. Recovery on seventh day of illness.

Case 5. T. E., male, white, aged 57. Admitted February 7, 1935. Lobar pneumonia. Onset two days prior to admission with pain but no chill. Sputum: pneumococcus Type II. Blood culture: negative. W. B. C., 28,900. Roentgen-ray: confirmatory. Four ampoules serum given within 24 hours after admission. Recovery by rapid lysis.

Case 6. D. K., male, white, aged 40. Admitted February 12, 1935. Postoperative lobar pneumonia, right lower lobe. Onset one day following herniorraphy. Sputum: pneumococcus Group IV in large numbers. Blood culture: negative. W. B. C., 17,600. Roentgen-ray: confirmatory. Serum started first day. Six ampoules serum given. Recovery by rapid lysis.

Case 7. N. K., male, white, aged 55. Admitted February 18, 1935. Lobar pneumonia, right lower lobe. Typical onset one day prior to admission. Sputum: pneumococcus Type III. Blood culture: negative. W. B. C., 13,000. Roentgen-ray: confirmatory. Four ampoules serum given within 24 hours after admission. Recovery by rapid lysis.

Case 8. J. M., male, white, aged 72. Admitted March 21, 1935. Lobar pneumonia, left upper lobe. Post-tuberculous fibrosis of both apices. Onset of pneumonia four hours prior to admission. Sputum: pneumococcus Group IV and some streptococci. Blood culture: negative. W. B. C., 28,350. Roentgen-ray: confirmatory. One ampoule serum given five hours after onset. Recovery by rapid lysis.

Case 9. M. B., male, black, aged 25. Admitted March 29, 1935. Lobar pneumonia, left lower lobe. Typical onset seven hours prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. W. B. C., 17,000. Roentgen-ray: confirmatory. Eight ampoules of serum given in 48 hours. Recovery by rapid lysis.

Case 10. G. B., male, white, aged 42. Admitted April 5, 1935. Lobar pneumonia, left lower lobe. Typical onset five hours prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. W. B. C., 22,000. Roentgen-ray: confirmatory. Eight ampoules of serum given. Recovery by rapid lysis. (Figure 1.)

Case 11. G. P., male, white, aged 35. Admitted April 15, 1935. Lobar pneumonia, right upper and middle lobes. Nephritis. Chronic alcoholism with delirium tremens. Onset two days prior to admission, three days before serum. Sputum: pneumococcus Type I, few Vincent's organisms. Blood culture: negative. W. B. C., 23,350. Roentgen-ray: confirmatory. Urine: heavy albumin and many casts. Blood chemistry: N. P. N. 66 mg.; Urea N 54 mg. Eight ampoules serum in 28 hours. Rapid fall to normal in 24 hours. Temperature rose following day with development of marked delirium. Three more ampoules serum given. Developed marked bradypnea, cyanosis and some nuchal rigidity. Spinal fluid: increased pressure, but otherwise normal. Death on sixth day.

Case 12. Mrs. C. F., female, white, aged 35. First seen April 19, 1935. Lobar pneumonia, whole left lung. Empyema. Typical onset 28 hours before seen. Sputum: pneumococcus Group IV in great numbers. Blood culture: negative. W. B. C., 28,000. Roentgen-ray not taken (patient at home). Ten ampoules of serum given in 48 hours. Defervescence by gradual lysis to normal, followed by secondary moderate rise due to empyema. Pus from pleura: pneumococcus Type II. Thoracotomy with rib resection. Recovery.

Case 13. J. B., male, white, aged 31. Admitted April 20, 1935. Lobar pneumonia, left lower lobe. Typical onset two days prior to admission. Sputum: pneumococcus Type III. Blood culture: negative. W. B. C., 14,550. Roentgen-ray: con-

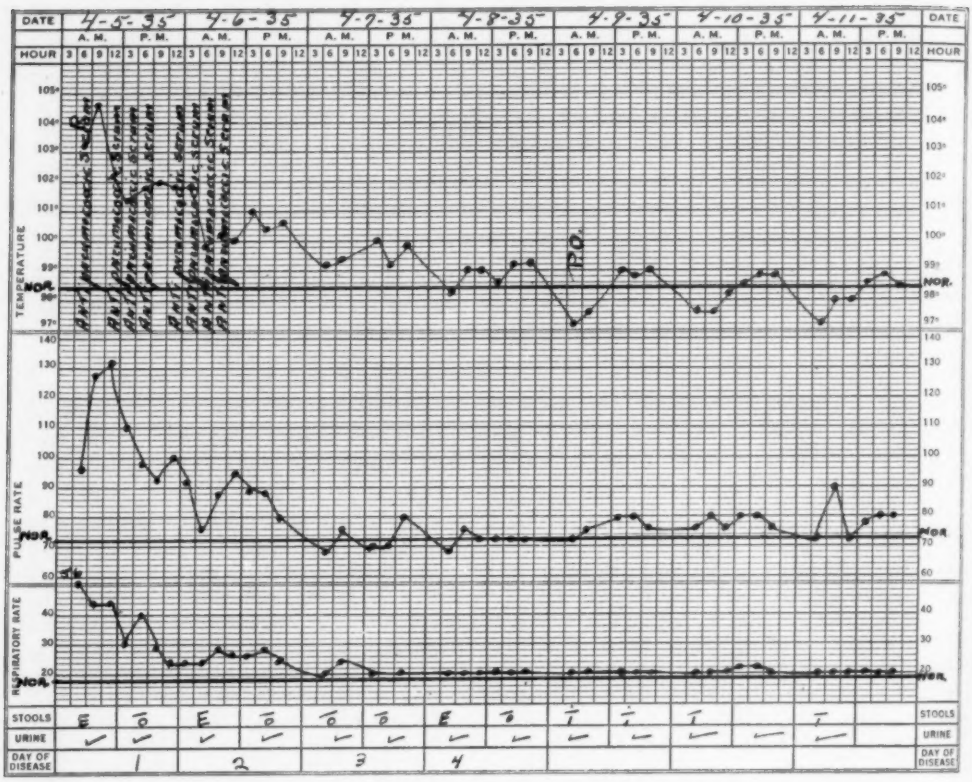

FIG. 1. Case 10, G. B. Lobar pneumonia, left lower lobe. Pneumococcus Group IV.

firmatory. Four ampoules serum given in 24 hours. Recovery by crisis in 24 hours. (Figure 2.)

Case 14. G. S., male, white, aged 64. Admitted April 22, 1935. Postoperative lobar pneumonia, whole left lung. Onset one day following herniorraphy. Sputum: pneumococcus Group IV. Blood culture: negative. W. B. C., 17,300. Roentgen-ray: confirmatory. Nine ampoules serum started 30 hours after onset and given within 30 hours. Recovery by rapid lysis within 30 hours.

*Case 15.** J. M., male, white, aged 58. Admitted April 27, 1935. Lobar pneumonia, left lower lobe. Typical onset 10 hours prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. W. B. C., 14,450. Roentgen-ray: confirmatory. Eight ampoules serum given within 48 hours. Recovery by lysis on fourth day.

Case 16.† W. H. J., male, white, aged 40. Admitted April 28, 1935. Lobar pneumonia, right lower lobe. Typical onset two days prior to administration of serum. Sputum: pneumococcus Type III. Blood culture: negative. W. B. C., 18,000. Three ampoules of serum given in 12 hours. Recovery by rapid lysis.

Case 17. C. G., male, white, aged 68. Admitted May 2, 1935. Lobar pneumonia, whole right lung. Chronic and acute alcoholism. Typical onset one day prior to admission. Sputum: pneumococcus Type III and many Vincent's organisms. Blood culture: pneumococcus Type III. W. B. C., 10,300. Roentgen-ray: con-

* Reported by kind permission of Dr. C. Wm. G. Schaefer.
† Reported by kind permission of Dr. John A. O'Donnell.

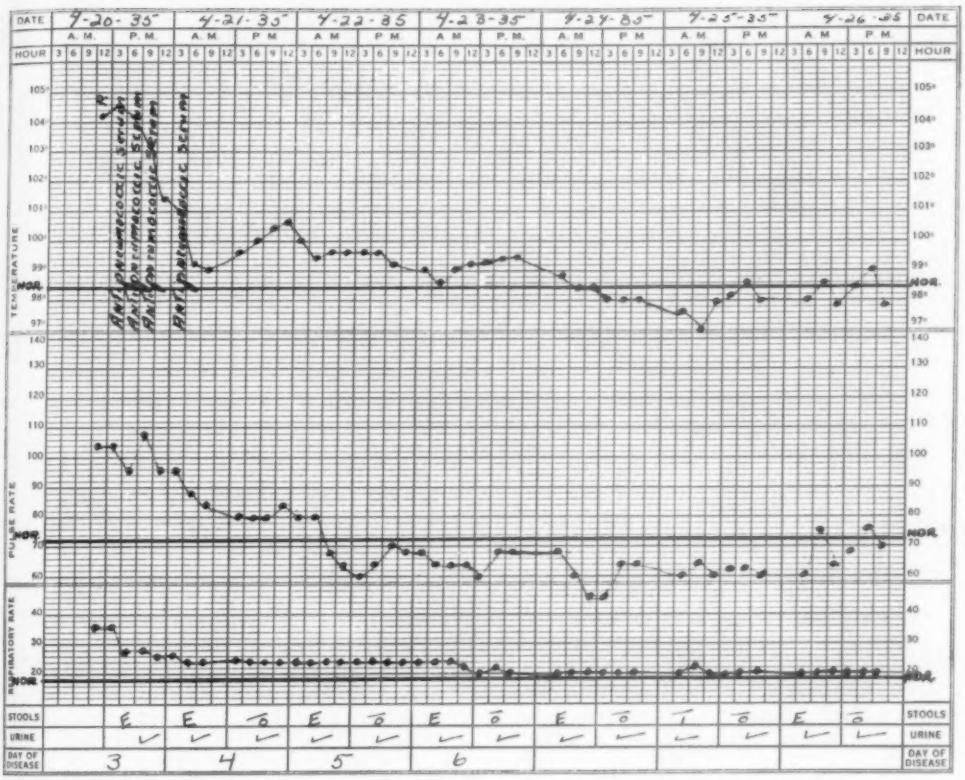

FIG. 2. Case 13, J. B. Lobar pneumonia, left lower lobe. Pneumococcus Type III.

firmatory. Eight ampoules of serum given in 48 hours. Death on eighth day. Autopsy: Lobar pneumonia. Right empyema, not diagnosed during life.

Case 18. F. M., female, white, aged 18. Admitted May 6, 1935. Lobar pneumonia, left lower lobe. Typical onset 36 hours prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. W. B. C., 26,500. Roentgen-ray: confirmatory. Seven ampoules serum given within 48 hours. Recovery by rapid lysis on fourth day of illness.

*Case 19.** S. A. W., male, white, aged 53. Admitted May 6, 1935. Lobar pneumonia, whole left lung; empyema. Onset three days prior to administration of serum. Sputum: pneumococcus Group IV. Blood culture: pneumococcus Group IV; showing 50, 50, 15, and 0 colonies per c.c. W. B. C., 29,750. Roentgen-ray: confirmatory. Eleven ampoules serum given over four days; interval of 40 hours between second and third ampoules of serum. Recovery by gradual lysis, with secondary rise due to empyema. Thoracotomy with rib resection. Recovery.

Case 20. G. Z., male, white, aged 21. Admitted April 30, 1935. Lobar pneumonia, whole right lung. Onset one day before admission with pain and bloody sputum but no chill. Sputum: pneumococcus Group IV and many streptococci. Blood culture: negative. W. B. C., 21,900. Roentgen-ray: confirmatory. Ten ampoules of serum given in 48 hours. Recovery by crisis on fifth day.

Case 21. N. R., female, white, aged 16. Admitted May 13, 1935. Postoperative lobar pneumonia, left hilus. Onset one day following appendectomy. Sputum: pneu-

* Reported by kind permission of Dr. J. R. Simon.

mococcus Group IV. Blood culture: negative. W. B. C., 25,000. Roentgen-ray: pneumonia, left hilus. Four ampoules serum given within 24 hours. Recovery by rapid lysis.

Case 22. L. S., male, white, aged 54. Admitted May 27, 1935. Postoperative lobar pneumonia, right upper lobe. Onset with chill one day following prostatic resection. Sputum: pneumococcus Type III. Blood culture: negative. W. B. C., 25,150. Roentgen-ray: confirmatory. Ten ampoules of serum given in 48 hours. Recovery by lysis.

Case 23. R. S., Male, white, aged 72. Admitted May 28, 1935. Lobar pneumonia, right lower lobe. Typical onset two days prior to admission. Sputum: pneumococcus Type II. Blood culture: negative. W. B. C., 28,750. Roentgen-ray: confirmatory. Nine ampoules of serum given in 36 hours. Recovery by rapid lysis.

Case 24. J. M., male, black, aged 53. Admitted June 5, 1935. Lobar pneumonia, whole left lung. Onset three days prior to admission with fever, cough, pain, and bloody sputum, but no chill. Sputum: pneumococcus Type III, streptococci, Vincent's organisms, Leptothrix. Blood culture: negative. W. B. C., 45,300. Roentgen-ray: confirmatory. Ten ampoules of serum given in 48 hours. Recovery by lysis. After one week of practically normal temperature and well being, moderate fever again developed and roentgen-ray showed left lower lobe entirely cleared, but very dense shadow in left upper lobe and considerable infiltration of peribronchial variety in right upper lobe. Abscess, tuberculosis, or neoplasm suspected. Patient, upon his own insistence, left hospital before accurate diagnosis could be established.

Brief outlines follow of those cases which, after serum treatment was instituted, proved to be lacking in certain of the qualifications demanded for admission to the above series:

Case A. D. T., male, black, aged 24. Admitted November 26, 1934, with diagnosis of lobar pneumonia, right upper lobe. Onset about one week prior to admission with fever and pain, but no chill. Variable signs over right upper lobe. Sputum: pneumococcus Group IV and Vincent's organisms. Blood culture: negative. W. B. C., 10,000, 10,500, 10,100. Roentgen-ray: shadow over right upper lobe. Wassermann: 3 plus. Six ampoules serum given in first 48 hours with no effect. After 12 days in hospital, course of neoarsphenamine given and patient recovered by slow lysis. The finding of many Vincent's organisms in the sputum with negative blood culture, comparatively low leukocyte count, lack of any noticeable effect on the course from serum administration in contrast to gradual defervescence over a period of three weeks under neoarsphenamine administration, might well justify a diagnosis of pulmonary spirochetosis rather than pneumococcus pneumonia.

Case B. C. D., female, white, aged 22. Admitted February 6, 1935. Postoperative lobar pneumonia, left lower lobe. Onset probably one day following biopsy and cauterization of cervix. Sputum: not sent until one week after recovery, when it showed streptococcus. Blood culture: negative. W. B. C., 12,500 on fifth day postoperative. Roentgen-ray: confirmatory. Serum started on fourth day postoperative. Three ampoules serum given. Recovery on sixth day postoperative Although physical signs and roentgen-ray evidence of pneumonia were present and response to serum administration was typical, there is no proof that this pneumonia was due to pneumococcus infection.

Case C. H. M., male, white, aged 17. Admitted March 6, 1935. Lobar pneumonia, left lower lobe. Marked malnutrition. Delirious on admission. Onset two days prior to admission. Sputum: bedside direct smear, pneumococcus (?). Blood culture: negative. W. B. C., 23,100. Roentgen-ray: confirmatory. Urine: heavy albumin and much pus. Six ampoules of serum given. Death in 45 hours. While pneumococci were thought to be present in the sputum at bedside examination, no

laboratory confirmation of this finding is available. Moreover, inasmuch as the urine was reported to contain a heavy cloud of albumin and a large quantity of pus, it is quite possible that this patient may have been suffering from generalized infection secondary to disease in the genito-urinary tract.

Case D. J. S., male, white, aged 18. Admitted March 9, 1935. Lobar pneumonia, right upper and lower lobes. Right empyema. Bronchopneumonia and fibrinous pleurisy in left lung. Onset five days prior to admission. Sputum: pneumococcus Group IV. Blood culture: negative. Culture from empyema: hemolytic streptococcus. W. B. C., 22,000. Roentgen-ray: confirmatory. Nine ampoules serum given within 48 hours after admission with no apparent effect. Recovery by lysis after surgical drainage. Even though Group IV pneumococci were recovered from the sputum, there was evidence of fluid in the right chest on admission, hemolytic streptococci rather than pneumococci were recovered from the pleural exudate, and defervescence gradually occurred after drainage of the empyema. The streptococcus infection was probably dominant.

Case E. H. G., male, white, aged 22. Admitted March 9, 1935. Lobar pneumonia. Loculated empyema and fibrinous pericarditis. (These present on admission.) Onset with chill four days prior to admission. (This information questionable.) Sputum: pneumococcus Group IV. Blood culture: pneumococcus Type II. Pleural fluid: pneumococcus Type II. W. B. C., 20,000. Roentgen-ray: confirmatory. Seven ampoules serum given. Several aspirations of chest. Death 48 hours after admission. Autopsy: confirmed clinical findings. Due to the fact that the empyema was loculated, adequate drainage could not be obtained.

Case F. H. R., male, white, aged 31. Admitted May 9, 1935. Lobar pneumonia, whole right lung. Typical onset two days prior to admission. Sputum: pneumococcus Group IV, tubercle bacilli, Vincent's organisms. Blood culture: pneumococcus Group IV. W. B. C., 18,150. Roentgen-ray: confirmatory. Twelve ampoules serum in 48 hours. Recovery from pneumonia by slow lysis. Sent to tuberculosis sanatorium.

Case G. W. R., male, black, aged 48. Admitted May 16, 1935. Lobar pneumonia, whole left lung, right upper and middle lobes. Active pulmonary tuberculosis. Diabetes mellitus. Typical onset one day prior to admission. Sputum: pneumococcus Group IV and many tubercle bacilli. Blood culture: negative. W. B. C., 15,950. Roentgen-ray: confirmatory. Urine: sugar 4 plus. Blood sugar: 308 mg. Nine ampoules of serum given in 48 hours. Temperature fell by crisis on seventh day; however, a secondary rise associated with symptoms of meningeal irritation occurred two days later, and death occurred on eleventh day. Spinal fluid: globulin 1 plus; 60 cells, mostly lymphocytes. Autopsy: lobar pneumonia as above, pulmonary tuberculosis.

Case H. A. C., male, black, aged 60 (?). Admitted July 8, 1935. Lobar pneumonia, whole right lung. Onset three days prior to admission. Sputum: pneumococcus Type III. Blood culture: pneumococcus Type III. W. B. C., 50,000. Urine: sugar 4 plus, acetone and diacetic acid positive. Blood chemistry: N. P. N. 61.6 mg.; sugar 652 mg. Roentgen-ray: confirmatory. Three ampoules serum given in 15 hours; temperature, pulse, and respiration dropped rapidly to normal. However, patient became stuporous and comatose and temperature again rose and patient died of diabetic coma 24 hours after admission. Reports of blood chemistry and urine not received in time to institute treatment.

Comment

In the following discussion only the 24 cases of proved pneumococcus pneumonia admitted not later than the fourth day of their disease and not obviously complicated are considered.

One of the outstanding impressions received in observing this group of cases was the relative absence of symptoms and signs of severe toxicity. Although quite aware of the impossibility of accurately measuring manifestations of toxicity, we were struck by the low incidence of marked cyanosis, by the relatively low degree of respiratory embarrassment, the improved quality of the pulse, and the low incidence of delirium and tympanites after serum had been administered.

In evaluating specific therapy for an acute febrile illness of known duration, one of the most important factors is its ability to shorten the course of the disease as well as alter its severity. From a review of the above case abstracts this property of the serum is strongly suggested. It may be rightfully objected that an occasional case of pneumonia may terminate in less than the classical seven days; yet one could hardly anticipate this in as high a percentage of cases as occurred in this series. Of the 24 fully qualified cases which were serum treated, 16 (numbers 2, 3, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 18, 20, 21, and 23) recovered by rapid lysis or crisis.

No mortality statistics on the basis of so limited a series warrant any definite conclusions. Experience with the treatment of this disease shows that its mortality varies from season to season and even from month to month. It may be remarked, however, that the death rate from pneumonia in Pittsburgh is always comparatively high; in fact it is usually not exceeded by that in any other of the large cities of the United States. It is equally impossible to maintain adequate control in estimating the value of a curative agent because the number of variables, such as age, virulence of infection, degree of blood invasion, previous state of nutrition and health, stage of disease upon admission, etc., is legion. Nevertheless a comparison of the mortality rate in this series and that in a group of approximately the same number which were treated in this hospital at about the same time without serum is interesting and, we believe, suggestive. The control series was comprised of those proved cases of pneumococcus pneumonia without obvious complications which either entered the hospital in the few weeks before the trial of serum treatment was initiated or during the periods when our supply of serum was exhausted; those which were admitted later than the fourth day of the disease; and those which were private patients of other physicians in the hospital and not under our control. Most of these cases received small doses of quinine in addition to the hygienic and symptomatic treatment outlined above. Of 24 serum-treated cases three died, a mortality of 12.5 per cent. Of 26 cases * treated without serum 10 died, a

* Of these, one case which recovered, and one which terminated fatally were not typed. Excluded from the control series were one case complicated by pyelonephritis and phlebitis, one case by diabetes mellitus, one case by parturition, four cases by asthma, one case by pulmonary fusospirochetosis and lung abscess, one case by rheumatic arthritis, and one case by chronic heart disease with decompensation.

Thus far in the 1935 to 1936 pneumonia season ten additional cases have been serum treated, with nine recoveries (including three with positive blood culture) and one death. These will receive further analysis in a subsequent report covering the current season's experience.

Grateful acknowledgment is made to Miss Edith Culbert for valuable aid in the preparation of accurate records.

mortality of 38.5 per cent. It is true that the average age in the serum-treated group was 47 while that in the control group was 50. However, of five cases aged 60 or more in the serum-treated group one died, a mortality of 20 per cent; while of 10 cases above 60 years of age in the control group, six died, a mortality of 60 per cent.

Analyzing the mortality as to type, we find that of three cases of Type I infection treated with serum, one case died; of two cases of Type I infection in the control series, both recovered. There were no deaths among three serum-treated cases of Type II infection, while one case out of three in the control group died. Of particular interest is the comparison in the Type III and Group IV cases, against which the serum contains no type-specific protective antibodies. Of six cases of Type III infection in the serum-treated group, one died, a mortality of 16.7 per cent; while three cases out of eight in the control group died, a mortality of 37.5 per cent. One case out of 12 in the serum-treated series of Group IV infections died, a mortality of 8.3 per cent; while of 11 in the control series five died, a mortality of 45.4 per cent. This marked discrepancy in mortality in the latter two groups gives support to the thesis that heterophile antibody and skin test toxin neutralizing bodies are of considerable value in the control of these infections.

Of four serum-treated cases with positive blood cultures one died. Of nine cases with positive blood cultures in the control series four died. Parenthetically, it is interesting to note that of three fatal cases in the serum-treated series, only one had a positive blood culture; and of 10 fatal cases in the control series only four had positive blood cultures. As opposed to the 25 per cent mortality in the four cases with positive blood cultures in the serum-treated series, there were two deaths among 20 cases or a mortality of 10 per cent in the cases with negative blood cultures. Whereas, in contrast to the 44.4 per cent mortality among the nine cases with positive blood cultures in the control series, there were six deaths among 17 cases with negative blood cultures, a mortality of 35.3 per cent.

If all cases to which serum was administered, regardless of their qualifications, were taken into consideration, the series would consist of 32 cases with seven deaths, a mortality of 21.8 per cent. The Type I mortality would be unaffected. There would be four cases of Type II infection with one death. There would be two deaths among seven cases of Type III infection, a mortality of 28.5 per cent; and two deaths among 16 cases of Group IV infection, a mortality of 12.5 per cent.

If all cases treated without serum, regardless of complications, were included in the control series, the latter would consist of 36 cases with 17 deaths, a mortality of 47.2 per cent. The Type I mortality would be unaffected. There would be five cases of Type II infection with three deaths. There would be four deaths among nine cases of Type III infection, a mortality of 44.4 per cent; and eight deaths among 17 cases of Group IV infection, a mortality of 47 per cent.

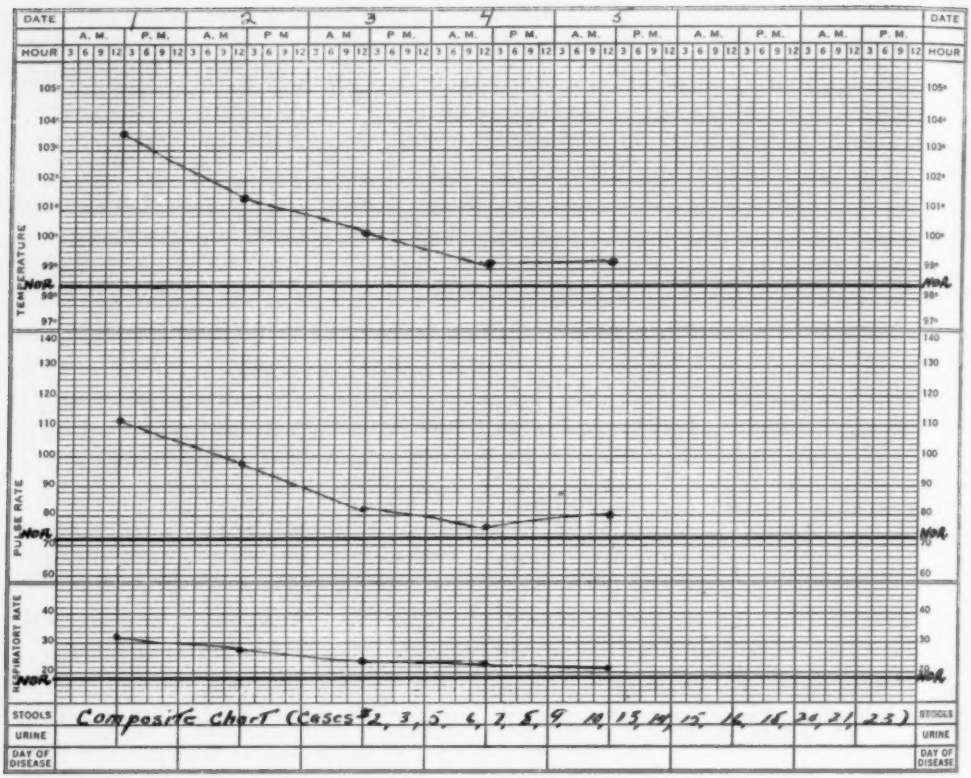

FIG. 3. Composite chart: Cases 2, 3, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 18, 20, 21, and 23.

It should be noted that, judging from the experience with this series of cases (cases number 12, 17, 19, and E), this serum given intravenously seems to have no anti-bacterial activity against pneumococci that have gained access to the pleural sac.

In the early days of the study serum was given at six-hour intervals. Later the interval was reduced to four hours with, we believe, better results. The number of ampoules given varied from one to twelve, the majority of cases receiving eight ampoules. Chill reactions were frequent in the early cases following administration of the first allotment of serum received, none of which, however, proved serious. Since that supply was exhausted such reactions have been remarkably rare. Serum sickness of the usual type, characterized by urticaria, joint pains, and low-grade fever occurred approximately one week after administration in 14, or 56 per cent, of the 25 cases which recovered.

As the most striking effect of the administration of this serum thus far observed appeared to be a prompt, premature defervescence, a composite chart (figure 3) was prepared by plotting the average daily temperature, pulse, and respiratory rate in 16 cases (cases number 2, 3, 5, 6, 7, 8, 9, 10,

13, 14, 15, 16, 18, 20, 21 and 23) responding by crisis or rapid lysis. The curve begins with the records immediately preceding the first dose of serum.*

The question of whether the outcome of the disease is influenced by the stage at which treatment is instituted cannot be answered from this study, since serum treatment was limited to cases admitted not later than the fourth day of their disease. Further investigation is necessary to determine whether this type of serum treatment has value in cases seen late in the course of their infection. The question of optimal dosage also requires further study.

Summary

Experimental observations of various investigators have been cited which indicate that the efficacy of the conventional type-specific antipneumococcus horse serum is enhanced by the addition of heterophile antibody and antibodies which have the property of neutralizing toxic substances in pneumococcus filtrates.

Experience with the use of such a modified antipneumococcus serum in the treatment of a series of 32 cases of pneumococcus pneumonia in Pittsburgh during the 1934 to 1935 season has been outlined and the results analyzed. Comparison has been drawn between the results in this series and those in a similar series treated without benefit of serum administration. While the series is relatively small and dogmatic conclusions therefrom as to effect on mortality are probably not warranted, certain deductions may, we feel, be reasonably drawn.

Conclusions

1. Serum-treated cases appear definitely less toxic than those not so treated.

2. The febrile course of a large percentage of cases of pneumococcus pneumonia of all types treated with serum was prematurely terminated.

3. The efficacy of the serum in Type III and Group IV cases is particularly striking as these infections have not been favorably influenced by the administration of the available conventional antipneumococcus sera.

4. Antipneumococcus horse serum modified by the addition of heterophile antibody and neutralizing antibodies for toxic substances in pneumococcus filtrates constitutes a promising new agent in the therapy of pneumococcus pneumonia.

BIBLIOGRAPHY

1. Statistical reports to date summarized by Belk, W. P.: The specific treatment of lobar pneumonia, Jr. Am. Med. Assoc., 1935, cv, 868.

2. Forssman, J.: Die Herstellung hochwertiger spezifischer Schafhämolysine ohne Verwendung von Schafblut. Ein Beitrag zur Lehre von heterologer Antikörperbildung, Biochem. Ztschr., 1911, xxxvii, 78.

* *Editor's note:* Charts of the temperature, pulse and respiration of the majority of the serum-treated cases were furnished by the author but lack of space forbade their publication.

3. Bailey, G. H., and Shorb, M. S.: Heterophile antigen in pneumococci, Am. Jr. Hyg., 1931, xiii, 831.
4. Finland, M., Ruegsegger, J. M., and Felton, L. D.: Heterophile antibodies in pneumonia, Jr. Clin. Invest., 1935, xiv, 683.
5. Bailey, G. H., and Shorb, M. S.: Immunological relationships of pneumococci and other heterophile antigens and biological significance in pneumococcus infections, Am. Jr. Hyg., 1933, xvii, 358.
6. Jamieson, W. A., and Powell, H. M.: Further studies on the immunology of the pneumococcus, Am. Jr. Hyg., 1931, xiii, 823.
7. Powell, H. M., Jamieson, W. A., Bailey, G. H., and Hyde, R. R.: A comparative study of antipneumococcus serum containing heterophile antibody, Am. Jr. Hyg., 1933, xvii, 102.

SOME FACTORS IN THE ETIOLOGY OF THE PSYCHONEUROSES *

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The first factor of importance in the understanding of the etiology of the psychoneuroses is that they are not clinical states in the sense of diseases but rather they are states of mind. These patients come to physicians for treatment, and their symptoms are usually referable to one of the bodily systems, but the physician must recognize that they represent not something which has happened inside the patient but something which has happened to the relationship of the patient to the world in which he has to live. Thus each psychoneurosis is an expression of the reactions of the individual toward certain factors of his life which he is unable to handle in a manner compatible with health.

One might well ask what has health to do with the reactions of a patient to his life's problems? It would have nothing to do with it were it not for the fact that sickness may be an asset to the patient. Sickness is incapacitating surely and takes one to the doctor, but often sickness likewise may have an asset value in that it serves as an excuse that permits one to neglect to do things that would be required of one who is well. The Monday morning headache of the child who has not prepared his home work is the prototype of many neurotic symptoms that may appear later in life—when again the needs of existence appear to be too much for one to meet. The asset element in many of the neurotic symptoms of adult life lies in the fact that they absolve one of the responsibility of acting like a normal healthy individual. We pity the sick, excuse them from many things and afford them special treatment, and it is just this special treatment that the neurotic is searching for with his symptomatology.

Within the scope of such a paper it would be impossible to go into the psychology of the psychoneurotic symptomatology. Here one can only draw the line, somewhat arbitrarily, between conscious, deliberate fabrication of symptoms in which the patient himself does not really believe—which is malingering—and the unconscious assumption of symptoms in whose reality the patient stoutly believes—which is neurosis. Charcot expressed this distinction in his famous dictum "The hysteric is a malingerer who does not lie." This succinct sentence expresses all that I have space to say before I go on to etiological factors.

The raison d'être then of the psychoneurosis is the fact that it permits the patient to escape from complete responsibility for himself. Responsibility to others and to the world in which we live is in good measure the product of civilization. The more complex our civilization the greater are

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the responsibilities of each individual member. One may refer it, as Trotter did, to the herd instinct; but whatever it is there can be no doubt that the average man can not live in comfort and happiness unless he has the good opinion of those in whose company he lives his daily life. We sum these factors up in the expression "public opinion," and each man must bask in some degree of that in order to preserve that good self opinion which is so essential to normal life.

The mores of the group may press most heavily upon an individual, but nevertheless he feels he must conform to them if he is to hold his head up among his fellows. There are ideals in public opinion which most of us feel we must at least compromise with even if we are not inclined to conform to them. There are those who feel this way about religious ideals but their number seems to have diminished in recent years. Even where this diminution has occurred not dissimilar ideals of an ethical and a social nature have taken their place with equal force. Ideals of decency and honesty, of fair dealing and "square shooting," of loyalty and honor, of duty and that rather vague thing which is spoken of as "social consciousness" are just as potent as those other similar ideals which are based on worship and reverence. The taboos attached to these social concepts may not be violated unless one is sick, and neurosis is one of the sicknesses that permit it. Not only must the violation not be in reality but it must not be even in the thoughts and wishes of the individual. Of this he is frequently more afraid than he is of any possible infraction in real life. The former is quite as damaging to self respect and, because it has never reached any real expression, it is all the more frightening and hence productive of neurotic symptoms.

Were life as simple as perhaps it should be, were all our motives as nobly inspired as we would like to have the world believe, no one would be beset with the sort of conflicts which form the basis for the psychoneuroses. Man is a social animal, but he is not only that. More fundamental than the social side of human life is the individual, selfish, egocentric side which expresses itself in the doctrine of "every man for himself and the devil take the hindmost," that determines much more of human conduct than do the social, altruistic motives of which we like to boast. This is the sort of conflict that calls for a resolution in every one of us. That resolution may be an adjustment of the personality compatible with health or, when it breaks down, a psychoneurosis. The individual and the social are often opposing forces which pull the erring human in many ways, and one, at least, of these ways leads to neurosis.

Man plays, at best, a dual rôle in many of his activities, and this would be of little consequence were it not for the fact that both ends of this duality are mutually incompatible. The more incompatible the components of this conflict the greater is the possibility of the conflict eventuating in a neurosis. Such a conflict as that between man as a decent member of a civilized society and man as a mammal, or between man as an idealistic social being and man

as a greedy individualist, requires considerable mental adjustment and adaptation to reach a level of solution. This solution may be one compatible with mental health—an adequate one such as most of us succeed in attaining and maintaining most of the time—or an inadequate one in which the need for sickness plays a part of varying importance. Such inadequate solutions may be benign or malignant. The benign reactions are those which permit the individual to lead something approximating a normal life even though a sick one, which is the psychoneurosis; while in the malignant reactions the patient has cast aside all pretense of a normal life to live in a world of his own fantasy, which is psychosis of the schizophrenic sort.

But we must confine ourselves to the psychoneurosis and try to outline some of the factors which stand in conflict with the social man. Primarily these are things of the instincts. One runs the risk of treading on debatable ground when one speaks of instincts. So much has been said and written on this subject that one can find a plenty of opinion either to establish or deny the importance of these primitive motives. This is not the place to indulge in such a controversy. We must assume merely that there are trends in human and other animal life which are not learned and which are common to most of the members of a species. By instincts one need mean little more than this.

It is convenient to divide instincts into two groups: (1) instincts of self preservation, and (2) instincts of preservation of the species. The former may be called the ego instincts and the latter the sexual instincts. In the discussion of the etiology of the neuroses the sexual instincts have played a very prominent rôle. Perhaps this may have been too prominent, but it is doubtful if this could be the case. It is doubtful if there exists in animal life a force more potent than sex. In defining sex one must not restrict the definition to those physical activities which tend to eventuate in the preservation of the species. The term sexual must cover all of those activities, physical and mental, which appertain to the phenomenon of human mating. Nothing is more interesting to the majority of the human race than this, and nothing occupies human thought to a greater extent. Plato's description of the sexual urge as "an imperious head-strong power" is as accurate today as ever. It is the motive most fitting of all to come in conflict with the ideals of a self conscious, repressed society. It is true that improper handling of sexual urges in a mind-bound society by inadequate individuals brings to us the majority of our psychoneuroses; but all psychoneuroses are not based upon sex.

The other instinct of self preservation is just as capable of producing psychoneurotic reactions when improperly handled as is the sexual, and it is of this group especially that I wish to speak. The instinct of self preservation is often of even less respectability than is the sexual. It tends to express itself in motives that may have even less of social value than the other. Such egocentric motives as fear and greed are potent forces in all of us but they are never pretty things. Most of us are even more ashamed of them

than we are of our sexual urges. Potent they are in individual life, but on the social plane they are frequently shameful, hence they are ideally fitted to form the basis for that sort of conflict in the personality that leads to neurosis.

Fear is a normal component of animal psychology. It is a direct expression of the instinct of self preservation. Not only is there fear of death which is but an expression of the wish to live, but there are other fears which constantly beset the individual in a civilized society. Fear of injury, fear of exposure and of shame, fear of loss of position and respect, fear of the future, both here and hereafter, and fear of the loss of the feeling of personal security are quite as competent causes of the psychoneurosis as is anything in the sexual life. Life is necessary for man, but even more necessary often, for civilized man, is comfortable life which is not possible without a high opinion of himself and an adequate measure of approval from public opinion.

Greed is another motive all too human. Frequently we like to call it by other more euphonious names especially when we see it in ourselves. It is difficult to appraise it accurately because it is so universal, and even when one sees it in very pure form, such as in some of the litigation and compensation neuroses, one does not like to call it by its real name. Maybe I should not use the word if I feel it calls for so much defense, but I know of no other that expresses so much of what I mean.

If this were all to the ego plane neuroses, just fear and greed, the problem would be simple indeed, but many other motives enter into the make-up. Euphemism and hyperbole play as important a part in the etiology of the psychoneurosis as they do in the symptomatology. Self-respect which is often only another name for conceit, justice which is often indistinguishable from revenge, and the desire for security which may be but a form of indolence may, any or all, enter into the causation of the ego neurosis and cloud the understanding of it with terms that are difficult to define. And when a money value can be placed upon the neurosis as in the compensation neurosis, and legalistic considerations enter into its interpretation, one is faced with a psychological problem of such complexity that simple direct thinking becomes well nigh impossible.

I had hoped in this paper to describe these ego-plane neuroses in which sexual factors play little if any part. They have been described as " situation neuroses " in an attempt to express the idea that situations in the environment of the patient play the more important rôle in the etiology. This is not altogether the case, for while it is true that external considerations hold a prominent place in the causation, yet the personality of the patient and his instinctive ego urges really do the work of formulating the neurosis just as they do the neuroses of sexual origin.

We saw the ego neuroses in their simplest and truest form in the war neuroses—the so-called " shell shock " of the World's War. Back of all of them lay the good old human mechanism of fear—that fear which we all felt

near the front. Some of these cases appeared in camps in this country and others in France at any point up to the front. The clinical picture was the same no matter where they were seen, for the primary cause was the same—fear, which hit different men at different places.

In civil life we have as frequent ego-plane neuroses the compensation-litigation neuroses with which you are all familiar. Usually these follow injury of some sort and hence are known as "traumatic neuroses." The nature and severity of the injury have nothing to do with the make-up of the neuroses. The one point they all have in common is that the injury is compensable. I have yet to see a patient with a traumatic neurosis which resulted from an injury sustained while working for himself.

In business life today ego-plane neuroses not infrequently develop. The present business depression is responsible in a way for some of them, but the ego motives of greed and fear of personal and financial insecurity still form the foundation stones of the etiology. It is interesting to note that the depression has not materially increased the number of our psychoneurotics. This is especially true of those people who are on relief. They have hit the bottom and have nothing left to fear. Life can become nothing but better for them, and on a ground work of such a psychology, psychoneurosis can not find soil to grow. They may become dulled and discouraged or they may become social radicals but the psychoneurosis is not a part of their reactions. It is usually those who still have hopes of surmounting their difficulties and eventually triumphing who hold in their makeup the capacity for psychoneurosis. This is especially true when compensation factors occupy a place in the general life picture. The following cases may illustrate some of the points which I have been trying to make.

Case Reports

Case 1. J. M., aged 58. This man, an uneducated Russian Jew, was brought to this country while still a small child and had been earning his own living since he was eight years of age. As a boy he went into the clothing business and worked his way up until he owned his own factory. He prospered and says he made a great deal of money, and during this time he took out a large amount of life and disability insurance.

In 1927 he began to feel badly but kept on with his work because he had always been a hard worker and knew of nothing else to do. He lost considerable weight and finally "collapsed" at his place of business. When examined by his doctor he was found to have diabetes; under treatment he improved. For the first few months he was able to spend only an hour or so a day at his work, and as a result his business suffered. By 1929 his business was in such bad shape that he decided to close it out, which he did without going into bankruptcy, paying his creditors in full. It is of interest to note that during these years of considerable incapacity he never made any claim upon his insurance company for compensation although he was clearly entitled to it. He felt secure in regard to the future and his ability to earn his living at his trade without relying on compensation. In 1930, after he had closed out his business, he took a position as a salesman with another clothing firm and did well. He continued to work hard, and his employers were sufficiently satisfied with him to renew his contract when it expired. Then something happened to business. He saw it melting away before his eyes. He had always been able to make good adjustments

in a world of good business, but he could find nothing to live by in a world of no business.

In June of 1931 he had what he describes as a "breakdown." He began to have headaches, pains all over, dizziness and general weakness. These symptoms became gradually worse until he had to give up his work after a few months. When I saw him in 1933 his complaints were dizziness, easy fatigability, headache, pains in his arms and legs, insecure gait and station and insomnia. The neurological examination was entirely negative. He was receiving disability compensation at the rate of $500.00 a month.

It was obvious that this man was suffering from a psychoneurosis and not from any organic disease of the nervous system. The question of how much incapacity he had is a difficult one to answer unless one could define "incapacity." He had no means of support except his compensation, and if this were withdrawn he probably could not find enough business to do to support him. Support was dependent on his being incapacitated. He could not do any work because he thoroughly believed he could not work. If his business would pick up he would probably be glad to get into it again and then would not need compensation. The fact that he did not ask for compensation when he was organically incapacitated with his diabetes proves that he was not of the sort of personality that malingers. His neurosis was caused by the business situation in which he found himself plus the compensation which gave him security and paid him well for staying sick.

Case 2. J. C., aged 47. This was an agitated, depressed looking man who came in complaining that he could not rest, that he worried all the time and felt a fog in his head. In order to understand the condition one had to go back into the history to learn something of the background of this man's development. He had been born in Italy, the eldest of 10 children. At 16 years of age he came to this country and immediately went to work. He always worked hard during the day and attended night school until he was 20 years of age. He was interested only in his work and his family and took his responsibilities very seriously. He supported his mother and helped his nine younger brothers and sisters to get an education, one of whom graduated from medical school. After his marriage he devoted himself to his family, and his only interest was in making money for the support and education of his children.

He prospered in the contracting business and built a number of houses, some of which he owned. Previous to the stock market crash of 1929 he owned two fifty-family apartment houses and six two-family houses as well as other property. Then came the crash of October 1929, which was the beginning of his troubles. He was in the market pretty heavily and when stock prices fell he wanted to sell out all his holdings, but his bankers and his brokers insisted that he hold on to them. They kept constantly calling on him to put up more money and this he did until he had no more left. From being a man of considerable property and a comfortable income he was reduced to absolutely nothing except the $130.00 a month disability compensation he received from an insurance company. Then he became depressed and agitated and constantly walked up and down in his home saying he did not know what he was going to do. At times he went around to his bank and complained to the officers that they had not treated him fairly, and they would send for his family to come and get him. On one occasion they called in the police to remove him.

He continued his worrying, slept badly and talked continuously about what fate had done to him. In October 1931 he was placed in a State Mental Hospital where he remained for a year. There he lost weight and did not improve mentally. When he returned to his home he was calmer but his general mental condition was unchanged.

The neurological examination was entirely negative. Psychiatrically he appeared depressed and somewhat indifferent and he talked only of the past and of his losses.

His stream of mental activity was somewhat underproductive. He did not show any persecutory trend except that he felt he had lost his money as much due to bad advice of bankers and brokers as to anything else, which undoubtedly was not a delusion. His orientation and memory were normal.

This man was suffering from a symptomatic depression of a psychoneurotic sort which is quite understandable when one thinks of what he had been through. It is not difficult to understand the make-up of this depression but it is not quite so easy to see what the outcome will be. As he is at the present time and as business is at the present time he is undoubtedly completely incapacitated. Whether he is permanently incapacitated or not probably depends much more on business conditions than upon himself. Should business pick up and this man be able to borrow some money, build houses and rehabilitate himself there is a good chance that he would recover completely. If prosperity does not return soon it is doubtful if he will ever again be a productive member of society.

If one could consider this man alone and not the social, economic and business situations, one would say that there was nothing in this man to incapacitate him. However, one must appreciate the fact that he is living in the world as it is today, and from that point of view one must say that this man is thoroughly incapacitated at the present time for living in the kind of a world we have in this country today. The compensation he receives is all the security he has at present. If that were taken from him he would most likely go into a deeper depression from which recovery would be most doubtful.

These two cases summarize much better than I can express otherwise the points I have been trying to make in this presentation.

SOLITARY ULCER OF THE ILEUM AND ULCER OF MECKEL'S DIVERTICULUM *

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REPORTS on solitary ulcer of the ileum and on ulcer of Meckel's diverticulum indicate such difficulty in diagnosis, as well as such high surgical mortality that we are endeavoring to present a clearer conception of the problems presented by these two conditions.

There are several excellent reports in the American literature on hemorrhage and perforation attributable to ulcer in or near a Meckel's diverticulum, but little has been written on solitary ulcer of the ileum. In the foreign literature is the paper of Oudard and Jean, who collected reports of 56 cases (37 of ileal ulcer and 19 of jejunal ulcer) in which they noted a 50 per cent mortality among patients whose ulcers were recognized and operated on, while the mortality was 100 per cent if the ulcers had perforated, or if they were not found at operation, or if operation was not undertaken. Aschner and Karelitz reviewed 32 reported cases in which an ileal ulcer was situated at the mouth of a Meckel's diverticulum, with 11 deaths in the 32 cases (34 + per cent mortality). Even relative to ulcer of Meckel's diverticulum, with or without localized evidence of inflammation, Johnston and Renner found reported four deaths in 32 cases (12 + per cent mortality). In some reports ileal ulcer has been confused with what is now recognized as regional enteritis. Recently we have become more alert to the possibility of this nonspecific inflammatory lesion of the small bowel and as a result we have encountered an increasing number of such cases in the past three years. It is only by clinically separating these various lesions, one from the others, that diagnostic accuracy in diseases of the small bowel can be improved. Knowledge that such conditions may exist serves to stimulate development of diagnostic criteria and finally efforts toward working out of the etiology. The importance of thinking of ileal ulcer or of ulcer in Meckel's diverticulum, in contradistinction to regional enteritis, lies not so much in diagnosis as in surgery; usually, the area of enteritis is readily located whereas an ileal ulcer may be accompanied by so few signs of peritoneal involvement as to be found only by very careful exploration of the bowel.

Our study is based mainly on the surgical records of 10 patients who had solitary ulcer of the ileum and of eight patients who had ulcer of Meckel's diverticulum. There are many points common to both conditions but it is simpler to discuss them separately. In addition, we have obtained data from records of necropsy.

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Solitary Ulcer of the Ileum

There should be more reports on ileal ulcer than now are available. The feeling has existed that it is futile to diagnose lesions of the small bowel, and there has been a tendency to advise either to "observe further" or to "explore the small bowel." In diagnosis of chronic obstructing lesions, the roentgenologist has been of much assistance. But ileal ulcer is a clinical problem; roentgenology, as well as laboratory aids, has been chiefly of negative value in ruling out other conditions. The one exception, relative to laboratory aids, is detection of occult blood in the stool, which, if proper precautions are observed, is of real diagnostic value.

In reviewing the records of necropsy of The Mayo Clinic for the past 15 years, data were found on only one case in which death had been caused by perforation and bleeding of an ileal ulcer. This patient, a paretic, was in a hospital for the insane, and was apparently in fair physical health until he complained of vague abdominal pain which culminated abruptly, in 24 hours, with a rapidly fatal hemorrhage from the bowel. At necropsy an ulcer was found in the ileum, 80 cm. from the ileocecal valve. In examination of three other subjects, who had died of debilitating or infectious diseases, a small superficial ileal ulcer was found but seemed to be only incidental. In examination of a fifth subject, who had died following ileosigmoidostomy, an ileal ulcer was found six inches (15 cm.) from the ileocecal valve. This patient had been operated on in the "pre-liver days" in the hope of benefiting his pernicious anemia by excluding the colon. Apparently similar ileal ulcers, either single or multiple, have been observed occasionally in examination of subjects who had died of pernicious anemia, aplastic anemia or leukemia. The records of necropsy disclosed only one case of solitary jejunal ulcer, excluding the cases in which jejunal ulcers were associated with antecedent gastroduodenal operations. This one case was that of a patient the primary cause of whose death was Hodgkin's disease and who also suffered from psoriasis. At necropsy, a perforating jejunal ulcer was found which contributed to the final outcome. (These five cases are not included in table 1.)

Among our surgical records we have found none of a case of solitary jejunal ulcer not associated with gastric surgery. In their comprehensive review, Oudard and Jean discussed 53 cases of ulcer of the small bowel which they had collected from the foreign literature and added three of their own. They found 37 cases of solitary ileal ulcer and 19 of jejunal ulcer. Barber, in 1926, reported a case of acute perforation of a jejunal ulcer in which successful operation was performed. Other than this case, there is very little that we can find in the American literature on jejunal ulcer.

Clinical Notes. The 10 patients included in our clinical study of solitary ulcer of the ileum (table 1) consist of seven males and three females. Four of the patients were 24 to 28 years old; one, 35; three were 43, 47 and 47, respectively, and two were 58. Their symptoms covered a period of from

TABLE I
Summary of Cases of Solitary Ulcer of the Ileum

Case	Age, years, and sex	Duration of symptoms, years	Chief symptoms; site of pain	Nausea and vomiting	Stools		Blood			Preoperative diagnosis	Surgical findings; type of operation and date	Pathologic examination	Result
					Tarry	Occult blood	Hemoglobin, gm. per 100 c.c. or per cent	Erythrocytes, millions per cu. mm.	Leukocytes, per cu. mm.				
1	58 M.	3	Attacks of severe epigastric pain. Many mild attacks	Once	0	Test not done	*	*	*	Intestinal obstruction	Stricture lower ileum due to annular constricting ulcer which caused angulation and obstruction of ileum. Lateral anastomosis. 1917	No tissue	Well
2	58 F.	18	Increasingly severe attacks of epigastric pain culminating in constant pain in umbilical region	0	0	0	*	*	*	Chronic intestinal obstruction	Ulcer 3 feet from ileocecal valve producing marked dilatation of proximal ileum. Lateral anastomosis. 1918	No tissue	Well (?)
3	47 M.	3	Attacks of severe epigastric pain; worse shortly before admission. Pain extended through to back	+	0	0	*	*	*	Perforated peptic ulcer	Two inches proximal to ileocecal valve was perforated, ileal ulcer sealed off by coils of ileum. Contained several ounces of thin pus. Lateral anastomosis. Postoperative fistula needed repair. 1916	No tissue	Well

TABLE I—*Continued*

4	43 F.	4	Attacks of severe epigastric pain and tenderness in right lower quadrant. Pain extended through to back	0	0	Test not done	*	*	*	Ileocecal tumor	Ulcer in lower end of ileum causing obstruction. Lateral anastomosis. 1927	No tissue	Well
5	47 M.	8	Tarry stools every six months. Some gas and distention. No pain	0	+	+	7.0	3.5	7000	Bleeding lesion of small bowel	Spleen enlarged three to four times normal. Half way between duodenum and cecum, stricture due to annular ulcer. Dilatation of proximal ileum. Resection and anastomosis. 1930	Inflammatory annular ulcer containing lymphoid tissue	Well
6	35 M.	7	Attacks of sharp pain left to right at level of umbilicus. Pain extended through to back. Shortly before admission, weak and pale	0	+	+	7.3	3.13	6900	Bleeding lesion of small bowel	Ulcer 3 feet from ileocecal valve with dilatation of proximal ileum. Resection and anastomosis. 1935	Subacute simple inflammatory ulcer 1 cm. in diameter	Well
7	28 M.	5	Vague dyspepsia. Attacks of deep, bursting pain around umbilicus. Pain extended through to back	0	+	+	8.8	4.37	6200	Ileitis (?) Meckel's diverticulum (?) Duodenal ulcer (?)	Two feet proximal to ileocecal valve, angulated loop with obstruction. Resection and enteroanastomosis. 1934	Annular ulcer of ileum at mouth of a Meckel's diverticulum. No gastric mucosa in diverticulum	Well

TABLE I—*Continued*

Case	Age, years, and sex	Duration of symptoms, years	Chief symptoms; site of pain	Nausea and vomiting	Stools		Blood			Preoperative diagnosis	Surgical findings; type of operation and date	Pathologic examination	Result
					Tarry	Occult blood	Hemoglobin, gm. per 100 c.c. or per cent	Erythrocytes, millions per cu. mm.	Leukocytes, per cu. mm.				
8	26 M.	7/12	Attacks of abdominal pain which extended through to back. Weak; pale	+	None noted	+	30	3.5	6800	Lesion of small bowel	Solitary ulcer of ileum 2 feet proximal to ileocecal valve. Resection and anastomosis. Spleen enlarged to two times normal. 1927	Subacute simple shallow ulcer	Died third day after operation of peritonitis
9	26 M.	10	Some gas. Weak. Pale. "Catches" or pain in back; more marked in "attacks of weakness"	0	None noted	+	20	2.7	12000	Gastrointestinal hemorrhage	Previous splenectomy of 600 gm. spleen at mouth of a Meckel's diverticulum but in ileum an ulcer producing some obstruction of proximal ileum. Resection and anastomosis. 1930	Simple ulcer. Ileal mucosa in diverticulum	Well
10	24 F.	10	Anemia off and on for ten years. Lower abdominal cramps seven years. Worse shortly before admission and associated with nausea and vomiting	+	+	+	7.4	3.5	4000	Lesion of small bowel. Meckel's diverticulum (?)	Eighteen inches proximal to ileocecal valve was an annular stricture due to ulcer and causing obstruction. Resection and lateral anastomosis. 1932	Subacute annular constricting ulcer	Died of postoperative complications; abscess with peritonitis

* Normal.

seven months to 18 years with an average of more than six years. In seven cases the first symptoms were moderate to severe attacks of abdominal pain which was situated in the lower part of the epigastrium, around the umbilicus, or in the right lower quadrant. The pain was described as cramping, colicky, or as a deep, bursting pain usually accompanied by nausea and vomiting. The degree of pain eventually was found to be related to the degree of inflammation and obstruction. In five cases the pain extended into the small of the back or to the region between the shoulders. In addition to the attacks of pain, there was an irregular type of dyspepsia which had vague features of peptic ulcer, cholecystitis, or appendicitis. Taking of food sometimes initiated the distress, or again seemed to relieve it, while alkalies afforded no constant relief. One patient related that his appendix had been removed without improvement resulting. Another had undergone abdominal exploration, but the abdomen had been closed again; a report had been given the patient that there was a mass in the lower right portion of the abdomen, and anti-syphilitic treatment had been advised. A third patient said that cholecystostomy had been of no avail. A fourth, in whose case splenic anemia had been diagnosed, received no benefit from splenectomy. Of three patients, whose earlier symptoms were pallor and weakness, two had passed black, tarry stools, while the most anemic patient had not been aware of gross loss of blood from the bowel. One of these three eventually had attacks of lower abdominal cramp associated with nausea and vomiting, although the other two had only mild distention from gas, with no symptoms of moment other than the anemia.

Undoubtedly the striking symptom in six of the 10 cases was the severe secondary anemia, which was evidenced by a concentration of hemoglobin ranging from 20 to 55 per cent and a number of erythrocytes ranging from 2,700,000 to 4,370,000 per cubic millimeter of blood. The stools of all six patients were found to give a positive test for occult blood. Four had been aware of bleeding from the bowel, but of greater moment are the two, the value for whose hemoglobin was 20 per cent and 30 per cent, respectively, who had not known of any loss of blood. In examination of three patients, associated splenomegaly was found and this led to the possible diagnosis of splenic anemia; one of the patients, as has been noted above, had undergone splenectomy.

In all instances, aside from anemia or blood in the stools, the laboratory data were negative.

Surgical Findings. Surgery, for the type of ileal ulcer that we have encountered at the clinic, has had a more favorable outcome than that related in other reports which have been based on a series of cases in which the preponderance of ulcers has been of the perforating type. In our 10 cases, there were two postoperative deaths attributable to peritonitis secondary to the surgical difficulties but not attributable to preëxisting general peritonitis. In both fatal cases, that portion of the ileum which contained the ulcer had been resected. In four of the cases in which the results were successful

resection was performed, while in the remaining four, anastomosis around the obstructed portion sufficed to effect cure. In one of the latter four cases, the patient remained well for seven or eight years, at the end of which period her physician reported that she was again suffering some abdominal difficulty, the exact nature of which is not known to us.

Notes on Pathology. In nine of the ten cases the ulcer was situated from 2 to 36 inches (5 to 91 cm.) proximal to the ileocecal valve. In the tenth instance it was estimated to be in the ileum about half way between the duodenum and the cecal end. In nine of the 10 cases there was more or less evidence of dilatation and thickening of the ileum proximal to the ulcer. In none of the cases was there record of enlarged lymph nodes in the mesentery. Of the six specimens available for microscopic study, three (figures 1 and 2) were described as merely " subacute simple ulcers " about 1 cm. in diameter, while the other three were classified as " annular constricting ulcers " (figures 3 and 4). In one of these, much lymphoid tissue was noted but in none was any heterotopic tissue found. Evidences of tuberculosis were not found. The significance of these pathologic findings lies chiefly in the fact that it is a simple ulcer of the small bowel which may produce bleeding, perforation, or obstruction just as is true of peptic ulcer. All of the six ulcers of the patients who had been bleeding were resected, whereas in four cases the element of obstruction without demonstrated hemorrhage or anemia led to the simpler procedure of lateral anastomosis around the obstructing portion.

In two cases the ulcer was situated in the ileum, at the mouth of a Meckel's diverticulum, which raises the question if the ulcer was related to possible heterotopic mucosa in the diverticulum, such as was reported in the comprehensive study by Aschner and Karelitz. They reported two cases in which the patients were infants and found in the literature reports of 21 other cases in which gastric mucosa was present in the diverticulum; also they included 12 additional cases, in which, however, microscopic study of the diverticular mucosa had not been made. They postulated that since gastric mucosa of Meckel's diverticulum can secrete acid and ferments, stimulation of this heterotopic mucosa may be a factor in producing the ileal ulcer. In our case 7 (table 1), examination of the diverticular mucosa gave no evidence of the presence of gastric mucosa (figure 5) but only ileal mucosa. In case 9 (table 1) there was likewise only ileal mucosa, which gave evidence of chronic inflammation and subacute superficial ulceration. Although these are the only cases in our series in which Meckel's diverticulum occurred, it does seem as if the ileal ulcer was the chief lesion and the diverticulum was merely incidental. This evidence is not offered as against the possible relationship of heterotopic gastric mucosa to an ileal ulcer at the mouth of the diverticulum but merely to justify these two particular cases as examples of solitary ulcer of the ileum.

From another angle, and anticipating the second section of our paper, none of the eight patients who had inflamed, hemorrhagic Meckel's divertic-

ula had ulcer of the ileum although in five of the eight cases, gastric mucosa was found in the diverticulum. Hence, in our cases in which gastric mucosa was found in the diverticulum an ulcer had not developed in the adjacent ileal mucosa.

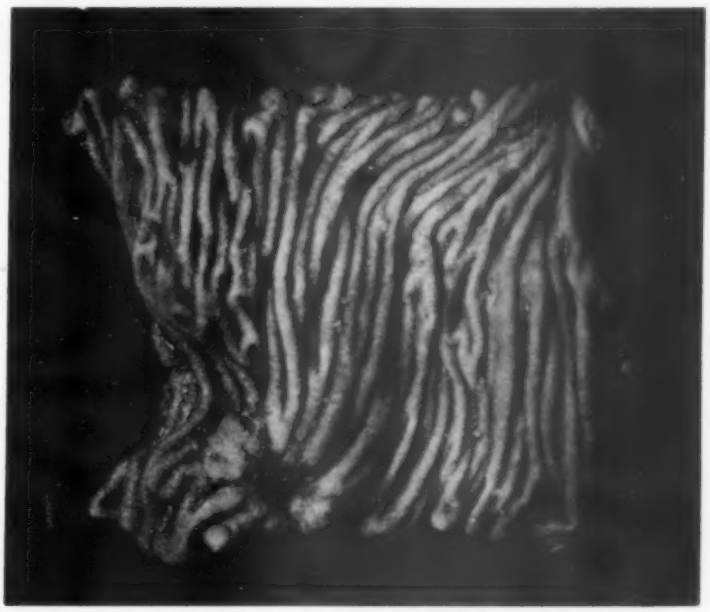

FIG. 1. (Case 6, table 1) Subacute, simple ulcer of ileum, measuring 1 by 1 cm.

FIG. 2. (Case 8, table 1) Subacute, simple ulcer of ileum, measuring 2.5 by 1.5 cm.

Comment. The problem of solitary ulcer of the ileum has been tersely stated by Moiroud: "Its pathology is obscure; its symptomatology is indefinite; and often perforation with peritonitis is its first revealing sign." Concerning our few cases, the last phrase could be changed to read, "and often secondary anemia with or without abdominal pain is its first revealing sign."

FIG. 3. (Case 10, table 1) Subacute, constricting, annular ulcer of ileum.

The various theories that have been advanced in explanation of the cause of peptic ulcer have been brought forth for solitary ileal ulcer but with no better conclusion relative to the one than to the other. In 28 cases of perforated ileal ulcer, Oudard and Jean noted that six of the patients had suffered severe abdominal injury and seven had undergone severe stress just prior to the onset of symptoms. No such history was obtained in our cases although there occurred no cases of acute perforation.

It is strange that the lower end of the ileum is, second to the duodenum, the most vulnerable portion of the small bowel. It is known that an ileal ulcer may develop when the error has been made of utilizing a loop of ileum rather than one of jejunum in the establishment of a gastro-enteric stoma. Likewise, most of the Meckel's diverticula are in this last 3 feet (91 cm.) of ileum. All but one of 12 ileal ulcers (two seen at necropsy, not included in table 1, and 10 at operation) were found in this segment. Is it possible that this portion is more vulnerable because the gradient of the entire bowel

FIG. 4. (Case 10, table 1) A section of the ulcer represented in figure 3.

is lowest at this point? [1] May heterotopic tissue exist in the ileum as it does in some Meckel's diverticula? While this theory has been suggested, it does seem logical, as one would expect, that the ulcer should heal spontaneously after destruction of the heterotopic cells and that it should not persist as a chronic ulcer.

FIG. 5. (Case 7, table 1) Ulcer in ileum at mouth of a Meckel's diverticulum which contained ileal mucosa.

Another query is the following: Why is bleeding so common in these cases? Although ten cases are too few to permit of any conclusions, yet certainly secondary anemia was the striking symptom in two-thirds of this number. Also, how can one explain the associated splenomegaly which was present in three of the six cases in which bleeding occurred and which also was noted in two of the eight cases in which there were bleeding ulcers of a Meckel's diverticulum? No patient gave any evidence of hepatic damage, nor would there seem to have been enough infection in the ulcer to produce infectious splenomegaly. Dragstedt reported the case of a boy 17 years of age who was found to have an ileal ulcer at the mouth of a Meckel's diverticulum; in this case splenomegaly was noted but shortly disappeared after resection of the bleeding ulcer. The patient who has secondary anemia

usually is not found to have splenomegaly although it occasionally occurs in association with the primary hypochromic anemia of women.[10] We have the impression that secondary anemia as a result of long-continued loss of blood from the bowel may produce splenomegaly. Our data are not sufficient to support this but it may be that the size of the spleen has not been carefully noted in all cases. Even though splenomegaly may occur only infrequently, it is important to bear in mind so as to avoid making a diagnosis of splenic anemia and thereby lead to splenectomy. The rule of examining a series of stools for occult blood should help prevent this error. Experimentally,[7] splenomegaly has been produced as a result of chronic loss of blood from the gastrointestinal tract; myeloid metaplasia of the spleen was found to have occurred. This would seem analogous to the findings in our five cases in which splenomegaly occurred.

Ulcer of Meckel's Diverticulum

The incidence of Meckel's diverticulum is about 2 per cent, with males predominating in a ratio of 2:1. The number of diverticula which produce symptoms is not easy to estimate. They may be a factor in obstruction, by invagination with resulting intussusception, by producing a twist or by ensnaring a loop of bowel, especially if a remnant of the vitelline duct remains. Others of these diverticula may undergo inflammatory change with resulting hemorrhage or perforation. Johnston and Renner collected the data on 78 cases of this type. There was microscopic proof of heterotopic mucosa in the diverticulum in 64 cases, in 50 of which definite ulceration was present. In the remaining 14 cases there was gross evidence of ulcer but microscopic examination was not made. Three-fourths of the 50 patients who had ulcers had suffered from bleeding from the bowel, and three-fifths of the 50 gave evidence of varying degrees of perforation.

Our knowledge of this condition is again obtained from records of operation and of necropsy. Data concerning the latter are not included in table 2, but from study of them Carlson has just completed a thesis on Meckel's diverticulum which covers the experience of the past 10 years. His study concurs with previous reports as to the incidence of 2 per cent and as to the 2:1 ratio of males to females. In 27.6 per cent of his 152 cases heterotopic tissue was found. Mucosa from various parts of the gastrointestinal tract was found in any and all combinations, or identification was made of a single type of mucosa from some one part of the tract from the cardia to the colon; one diverticulum even contained only islets of Langerhans. In none of the 152 cases was there evidence of ulceration, nor was the diverticulum related to the cause of death.

In surgical records of the corresponding 10 years 85 cases of diverticulum were noted. In 30 instances the surgeon merely recorded the abnormality as an accidental finding and the pouch was not removed. In 47 of the 55 cases in which diverticula were resected, there was reason to think

TABLE II
Summary of Cases of Hemorrhagic Ulcer of Meckel's Diverticulum

Case	Age, years, and sex	Previous surgery	Duration of symptoms, years	Pain	Nausea and vomiting	Stools		Blood			Pre-operative diagnosis	Surgical treatment; date	Pathological report on diverticulum	Result
						Tarry	Occult blood	Hemoglobin, gm. per 100 c.c. or per cent	Erythrocytes, millions per cu. mm.	Leukocytes, per cu. mm.				
1	6 M.	Appendectomy; benefit	1/3	None	0	+	Test not done	12.6		8000	Meckel's diverticulum (?)	Resection for diverticulitis. Enteroanastomosis. 1933	Gastric mucosa with diverticulitis.	Well
2	7 F.	Appendectomy; no benefit. Resection part of ileum; no benefit	5	Attacks of diffuse abdominal pain	Not known	+	Test not done	46	3.3	8300	Meckel's diverticulum or polyp	Resection for diverticulitis 10 inches from ileocecal valve. 1926	Gastric mucosa with chronic inflammation	Well
3	9 F.	None	1	Severe attacks of pain lower quadrant and umbilical region	+	+	Test not done	13.7	5.38		Lesion of small bowel	Resection for diverticulitis. 1930	Gastric mucosa with inflammation	Well
4	15 M.	Appendectomy; benefit	12	Attacks of epigastric pain	+	+	+	66	3.69	8300	Lesion of small bowel	Resection for diverticulitis 18 inches from valve. Splenomegaly (grade 1+). 1926	Diffuse diverticulitis with gastric mucosa but no acid cells	Well
5	22 M.	None	9	None. Mild aching right lower quadrant	0	+	Test not done	17.2	4.94		Meckel's diverticulum	Resection for diverticulitis 36 inches from valve. 1935	Ulcer at base containing polypoid gastric mucosa	Well

TABLE II—*Continued*

Case	Age, years, and sex	Previous surgery	Duration of symptoms, years	Pain	Nausea and vomiting	Stools		Blood			Pre-operative diagnosis	Surgical treatment; date	Pathological report on diverticulum	Result
						Tarry	Occult blood	Hemoglobin, gm. per 100 c.c. or per cent	Erythrocytes, millions per cu. mm.	Leukocytes, per cu. mm.				
6	30 M.	None	24	Vague symptoms of ulcer. Pain right lower quadrant three days before admission	0	+	Test not done	12.1	3.05	6400	Subacute appendicitis	Resection of ileum with marked inflammatory diverticular mass. Appendectomy. 1935	Diverticulitis of ileal mucosa	Well
7	44 F.	Appendectomy and cholecystectomy; no benefit	10⅔	None. Vague abdominal distress	0	+	+	37	2.18	4000	Duodenal ulcer	Resection for diverticulitis 24 inches from valve. Spleen resected (235 gm.). 1935	Jejunal mucosa	Well
8	61 M.	None	10	Severe abdominal pains	+	+	Test not done	48	4.46	18500	Obstruction small bowel	Entero-anastomosis. Resection of diverticulum. Much inflammation (site not stated). 1930	Ileal mucosa with marked inflammation	Well

that the diverticulum might be related to the patient's complaints. These diverticula varied from the definite type, such as a large pouch filled with hard feces and impacted in the pelvis, to the smaller, more innocent appearing off-shoots, resembling segments of normal ileum, which were removed in the course of eliminating all possible sources of trouble. Kernohan, of the Section on Surgical Pathology, has studied for us this group of 47 diverticula. He reported as follows: normal ileal mucosa, 15 cases; inflammatory ileal mucosa, 22; excess lymphoid tissue in ileal mucosa, 1; excess lymphocytes in ileal mucosa, 1; gastric mucosa with acid cells, 3; and gastric mucosa (one containing carcinoma), 5.

These data would not suggest that diverticula which contain heterotopic mucosa are more likely than others to undergo inflammatory change. As previously has been noted, Carlson found 27.6 per cent of healthy heterotopic tissue in otherwise normal diverticula while in this smaller group of 47, which were removed because possibly they explained the patients' symptoms, only 16 per cent contained heterotopic tissue. Probably of considerable importance is the group of 22 patients in which varying degrees of inflammatory reaction were observed. This will constitute part of a further study in our endeavor to learn more about the symptomatology and diagnosis of diseases of the small bowel.

Clinical Notes. The remaining eight cases of the 55 (table 2) are those of particular interest because they were characterized by secondary anemia and bleeding from the bowel. These are the eight cases mentioned in the introduction to this paper. Johnston and Renner found that 89 per cent of their 78 patients were 16 years of age or less. Although our group of eight cases is far too small to be comparable, yet it is of some clinical importance to note that half of the patients were more than 20 years of age (22, 30, 34, and 61 years), while the others were less than 16 years of age (15, nine, seven, and six years). The usual duration of symptoms was about the same in this group of cases as in those of ileal ulcer, ranging from four months to 24 years, although the average duration in the cases of diverticulum was higher (about nine years); the increase in the average duration is accounted for by the one patient who had some vague symptoms for 24 years but had not been ill enough to warrant operation until the recent development of more acute distress.

Bleeding from the bowel was the striking and constant finding in all eight cases, although on admission the blood count was normal in two because bleeding had not occurred for some time. Three of the eight patients made little or no complaint other than of weakness and of a history of dark to tarry stools. It will be recalled that in three of the 10 cases of ileal ulcer, anemia and weakness were the early or only symptoms of trouble.

In addition to the intestinal hemorrhages, five of the eight patients had suffered from attacks of abdominal pain. One located the pain in the epigastrium; one, across the lower part of the abdomen and around the umbilicus, and a third had pain in the right lower abdominal quadrant. In two

cases, pain was recorded only as "attacks of severe abdominal pain." In three of them, the pain was explained at operation as probably being attributable to partial obstruction, and in these cases nausea and vomiting had occurred.

Results of physical examination and laboratory findings were again meager, just as in the cases of ileal ulcer. In most instances, roentgenologic studies of the stomach and colon were made and, of course, abnormality was not found. Examination of the blood furnished one of the two objective positive findings and in six cases revealed secondary anemia of an extent depending on how recently hemorrhage had occurred. For no apparent reason the stools were examined for occult blood in only two cases and the test was positive in both.

Careful study of these eight patients, together with the apparent exclusion of disease of the upper and lower ends of the digestive tube, of a splenohepatic syndrome, and of blood dyscrasia, led to a fairly accurate diagnosis of "lesion or obstruction of the small bowel" in three instances and to an even more accurate opinion in three more that a Meckel's diverticulum probably was present. In case 7 (table 2) duodenal ulcer was held to be the most likely diagnosis and, in case 6 (table 2), subacute appendicitis. Neither of the last two was a grave error, as it was realized that surgical indications were present. It often has been emphasized that frequently it is impossible to be sure of the diagnosis, but of far greater importance is the nicety of judgment required to determine that a condition is surgical. This, in turn, emphasizes the responsibility of the surgeon to be prepared for, and to look for and to cope with, an unusual condition if all is not as was anticipated preoperatively.

As previously has been noted, the puzzling associated splenomegaly in two of the eight cases is of much interest. In one, hemorrhages had occurred 12 years prior to operation but no further gross bleeding was observed for the succeeding nine years. In the other case, gross bleeding had been noted for only the eight preceding months. On admission the concentration of hemoglobin was 66 per cent and 37 per cent, respectively. Probably the same explanation for the splenomegaly holds in these two cases as held in the three cases of ileal ulcer in which splenomegaly occurred.

Surgical Measures and Results. At operation the diverticulum in four cases was 10 to 36 inches (25 to 91 cm.) proximal to the ileocecal valve; in the remainder the site was not specified. In all, the diverticulum was resected and the ileal defect closed. In two cases, entero-anastomosis seemed advisable, for closure of the defect produced undue narrowing of the lumen. No deaths occurred and these eight patients had not had further trouble at the time of writing of this paper.

Notes on Pathology. Microscopic study of these eight diverticula revealed the following: (1) gastric mucosa with diverticulitis; (2) gastric mucosa with chronic inflammation; (3) gastric mucosa with inflammation; (4) diffuse diverticulitis with gastric mucosa but without acid cells; (5)

polypoid gastric mucosa and at its base a shallow, ulcerated area 5 mm. in diameter (figure 6); (6) ileal mucosa with marked inflammation of the diverticulum; (7) jejunal tissue, and (8) diverticulitis with ileal mucosa and ulceration of the entire mucosa.

Again, one is dealing with too few cases to permit conclusions, but it may be more than coincidental that five of these eight patients who suffered from intestinal hemorrhages were found to have inflammatory gastric mucosa in the diverticulum, and the diverticulum of one other contained jejunal mucosa.

FIG. 6. (Case 5, table 2) Meckel's diverticulum containing polypoid gastric mucosa, with ulcer at the base.

SUMMARY AND CONCLUSIONS

In none of 10 cases of solitary ulcer of the ileum was there found an associated Meckel's diverticulum containing gastric mucosa which might have been a factor in producing the ulcer. Of eight cases of inflammatory, hemorrhagic ulceration of a Meckel's diverticulum, in five gastric mucosa was found in the diverticulum and in one, jejunal mucosa. Possibly heterotopic mucosa is more likely to be found in cases in which bleeding is a feature. In contrast, in 47 additional cases in which a diverticulum had been resected, bleeding did not occur and only eight diverticula were found to contain gastric tissue. In 12 of the 18 cases there were sufficient clinical data to justify a preoperative diagnosis of a lesion of the small bowel. In three others the element of obstruction was outstanding and led to a diagnosis of intestinal obstruction. In two cases the condition was mistaken for peptic ulcer and in one, for subacute appendicitis.

Although definite clinical diagnosis is impossible, yet unexplained secondary anemia associated with a history of intestinal bleeding or with blood in the stools, and associated with roentgenologic evidence of a normal stomach and colon, should arouse the suspicion that there is an ulcer in the ileum or in a Meckel's diverticulum. Although attacks of midabdominal pain are customary, yet they may not occur. These observations should be sufficient to cause the clinician to advise surgical exploration. Hence there is need of close coöperation between clinician and surgeon in order that early diagnosis may lead to prompt surgical treatment. It should not be assumed that operation is urged on the evidence of a single intestinal hemorrhage or that all patients who have unexplained secondary anemia are too hastily subjected to exploration.

TABLE III

Condensed Data Concerning 18 Cases in Which Hemorrhagic, Ulcerative Lesions of the Ileum Existed

	Sex		Age, years	Pain	History of intestinal hemorrhage	Anemia	Occult blood in stool	Splenomegaly	Surgical result	
	Male	Female							Cured	Died
Solitary ulcer of the ileum (10 cases)	7	3	24 to 58	8	4	6	6*	3	8	2
Ulcer of Meckel's diverticulum (8 cases)	5	3	6 to 61	5	8	6	2†	2	8	

* No test made in two cases.
† No test made in six cases.

Pictures (table 3) of the two hemorrhagic, ulcerative lesions of the ileum which are the subject of this paper, represented by our 18 cases, may be described as follows:

Solitary Ulcer of the Ileum. Usually the patient is an adult aged 20 to 60 years, of either sex but more likely a male, who gives a history of having had attacks of abdominal pain for about six years. This pain is situated in the region of the umbilicus and often extends through to the small of the back or to the region between the shoulders. The patient usually is pale and although he may have been aware of intestinal hemorrhages, this is not always so, possibly because of minute, steady bleeding, lack of observation, or color blindness. Studies of the stomach, duodenum, colon, and liver are normal. The blood count may be normal but often discloses secondary anemia. The examining physician should exercise care not to be misled by the finding of an enlarged spleen. The test for occult blood in the stool is usually positive. Less often, the syndrome presented by a male, who has

secondary anemia, who has no abdominal distress, and all studies of whom give negative results, except for a positive test for blood in the stool, should suggest ileal ulcer.

Ulcer of Meckel's Diverticulum. The same general picture applies except that the age level is lower and that among children this condition rather than ileal ulcer is more likely to be the cause of tarry stools and anemia.

BIBLIOGRAPHY

1. Alvarez, W. C.: The mechanics of the digestive tract, 1922, P. B. Hoeber, New York, 192 pp.
2. Aschner, P. W., and Karelitz, S.: Peptic ulcer of Meckel's diverticulum and ileum, Ann. Surg., 1930, xci, 573–582.
3. Barber, W. H.: Ulcer of the jejunum, Ann. Surg., 1926, lxxxiv, 621–623.
4. Carlson, L. A.: Unpublished data.
5. Dragstedt, L. R.: Ulcus acidum of Meckel's diverticulum, Jr. Am. Med. Assoc., 1933, ci, 20–22.
6. Johnston, L. B., and Renner, G.: Peptic ulcer of Meckel's diverticulum, Surg., Gynec. and Obst., 1934, lix, 198–209.
7. Lange, F. J.: Myeloid metaplasia, Folia haemat., 1930, xliii, 95–120.
8. Moiroud, P.: Perforation d'un ulcère simple de l'iléom, Bull. et mém. Soc. nat. de chir., 1932, lviii, 1157–1162.
9. Oudard and Jean, G.: L'ulcère simple du grêle, Arch. d. mal. de l'app. digestif., 1925, xv, 208–228.
10. Witts, L. J.: Simple achlorhydric anemia, Guy's Hosp. Rep., 1930, lxxx, 253–296.

ERRORS IN THE INTERPRETATION OF CARDIOVASCULAR SYMPTOMS AND SIGNS *

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Errors often lead the way to new knowledge. Some of the most important advances in medicine have developed from the recognition and study of errors. Many details of our present rapidly progressing understanding of the diagnosis of cardiovascular disease have arisen from our analysis of errors in the interpretation of cardiovascular symptoms and signs. It is of some of these that I shall speak to you today.

The appraisal of cardiac symptoms, the most important part of cardiovascular examination and the part that requires no use of hands or instruments, is, and always has been, the most imperfect and neglected. Why this is so is strange, but it is a fact which cannot be overemphasized in the present state of medical training and practice. Too often the history of the patient is relegated to a relatively untrained person when it would be safer to turn over any other part of the examination. Or the physician is too hurried, or tired, or preoccupied to do a proper job. In ancient days the presentation of symptoms was usually too brief, leaving out important clues; in recent years there has been a tendency to bury the clues in a mass of details which are often irrelevant. The chronological development and relationships of the chief symptoms are the essentials which with past and family history permit in most cases a correct diagnosis of the cardiovascular condition, even before the physical examination is begun. I shall first present errors in the interpretation of the three chief cardiac symptoms—pain, dyspnea, and palpitation.

A. Symptoms.

1. **Pain.**

Mrs. E. C. M., 54 years old, housewife, entered the Massachusetts General Hospital on April 5, 1933, to have treatment for persistently recurring nocturnal heart attacks by paravertebral alcohol injection of the sympathetic nerve ganglia and rami.

Five years before she had begun to be troubled by momentary attacks of sharp, shooting pain originating just over the heart to the left of the sternum and radiating across the chest to the right and occasionally up over the left chest, almost to the clavicle. These transitory pains were not associated with exertion but seemed to come more when she was resting after a hard day and in the evening when in bed. She consulted her doctor who gave her tablets of nitroglycerine for the attacks, which seemed to give relief. This was at the time of the menopause. Ever since then this trouble had recurred at intervals, more frequently during the few weeks prior to her admission to the hospital, when she also noticed almost constant heartache, some dyspnea on hurrying, and blueness of her fingers and lips. Her ankles seemed to swell slightly at the end of the day. Her doctor digitalized her but she said that she had to omit the drug because of her inability to retain it.

* Read at the Detroit meeting of the American College of Physicians March 3, 1936.

About one year before entrance to the hospital she was troubled by another and more important symptom, consisting of precordial and substernal oppression in attacks at night awakening her and causing her to sit up, lasting for a few minutes at a time, and not responding quickly to nitroglycerine. On one occasion she was given morphine for relief. During the three weeks before entrance to the hospital these nocturnal attacks had increased in frequency and severity, and had been accompanied by a feeling of impending death, cold sweat, and rapid heart beat. She had, however, continued to do her housework as before.

Her past history revealed no important illnesses. She had six healthy children. Her mother and one sister had died of tuberculosis.

Physical examination showed a well developed and well nourished middle-aged woman with good color, normal breathing, no edema, and no abnormal neck pulsations. Her heart was normal in size, sounds, rate, and rhythm. There were no murmurs. The pulse rate was 80. The blood pressure varied from 154 to 165 millimeters of mercury systolic and from 90 to 100 diastolic. The lungs were normal.

Electrocardiogram showed normal rhythm and total inversion of Lead III.

Roentgen-ray examination showed some increase in the transverse diameter of the heart, which was recorded as greater than the long diameter.

The urine and blood were normal except for very slight albuminuria and slight secondary anemia. There was no bile in the urine. The stool was normal. The Hinton reaction was negative and the basal metabolic rate was minus 10 per cent.

On April 5, the day of her admission to the hospital, I saw her for a few minutes and wrote the following opinion: "Brief questioning does indicate the apparent occurrence of severe angina pectoris (decubitus) dating back three weeks (mild for two or three years before that). Examination shows no abnormalities except for slight hypertension. Further study—more careful history, electrocardiogram, roentgen-ray, Hinton reaction—are essential before final diagnosis. Paravertebral alcohol injection may well be indicated but I would advise postponing it for a few days until studies are completed. Try amyl nitrite for attacks." The surgeon wrote the following note in the record: "I believe that this patient is a suitable case for paravertebral alcohol block as her cardiac pain is so severe and she is getting so little relief from her medical measures. The only difficulty is the bilateral nature of the pain."

On April 7, 1933, we questioned her more carefully, realizing how rare severe angina pectoris is in a middle-aged woman with little or no hypertension and no story of substernal oppression on effort, and we gave the following verdict: "Further history this morning reveals the vitally important fact that rapid regular heart beating at more than twice the usual speed always accompanies the anterior chest discomfort and apparently precedes it. *This is extremely significant for it changes the diagnosis from coronary disease with angina pectoris to paroxysmal tachycardia with little or no heart disease.* . . . She is already better in here resting. Sedatives and quinidine sulphate (3 grains three times daily) will be much more likely to help her than any other drugs. I expect the Hinton reaction will be negative. For completeness we shall have a basal metabolic rate determination. Certainly there is no need at present for paravertebral alcohol injection unless the paroxysms grow very much worse and are refractory." One week later on the new therapy she was feeling very well, completely free of heart attacks. She was discharged from the hospital much improved on April 15.

Three months later, on July 3, 1933, she came to my office with no complaints except for very slight heart twinges for a second at a time on two days the previous week. She was taking quinidine. Examination including electrocardiogram and fluoroscopy showed nothing amiss except for slight hypertension (170 mm. systolic and 95 diastolic).

In October she reported the occurrence of a spell of racing of the heart lasting

a half hour after a recent fatiguing day. She had omitted the quinidine but thereupon resumed it. She no longer was afraid of the attacks—they had become simply disagreeable. Her blood pressure was 155 systolic and 90 diastolic.

I have continued to see this patient at intervals ever since, the last time on February 10, 1936, three weeks ago. She continued in good health (with infrequent palpitation) except for a series of acute attacks of typical gall stone colic with vomiting from August to November of last year (1935), completely relieved by the uneventful removal of her gall-bladder containing a large stone. She continued to have infrequent brief paroxysms of tachycardia up to the time of operation but none in the three months thereafter. The blood pressure continued to be slightly elevated (170 systolic and 95 diastolic on February 10, 1936). The electrocardiogram, including the chest lead, has been normal.

There are several morals to this tale. The most important one, of course, is the establishment by careful history taking of the correct diagnosis whereby the patient was not tagged with the label of a serious ailment and unnecessarily treated therefore. It is by no means the first time that such an error has occurred; I myself have encountered several other cases, the last one only a few weeks ago. The most notable patient of the sort that I recall was Jonnesco's first special case of supposed angina pectoris submitted to cervical sympathectomy who was still alive and in a good state of health many years afterwards; a review of the history of that case establishes this point.* There the history was all right but its interpretation was in error.

A second point of importance in this case is the change in the patient's reaction to the paroxysms of tachycardia. In a person untrained medically the first paroxysm of tachycardia usually causes great fear and discomfort; sometimes this happens even in a doctor. At such a critical time, or soon after, if a physician pronounces a verdict of heart disease and especially of angina pectoris, and warns against exertion and prescribes nitroglycerine, it is a very easy matter for the patient to develop a cardiac neurosis superimposed on the paroxysmal tachycardia. The palpitation due to the tachycardia becomes more disagreeable and in a nervously sensitive person even painful. The constant repetition causes a great dread and finally there is the addition of the fear of impending death and of a cold sweat at the time of the paroxysm, and of neurocirculatory asthenia with dyspnea and constant heartache and disturbed peripheral circulation between attacks, as in my case. When the patient is reassured and loses her fear of the attacks, only the disagreeable palpitation remains, and the fear of impending death and the cold sweat and other symptoms vanish. So it is, too, sometimes in the case of angina pectoris, although the more severe nature of this ailment more often justifies and causes these additional symptoms. As a matter of fact the great majority of my cases of angina pectoris have had neither the sense of impending dissolution nor cold sweating.

Here I would add an aside, namely, that there are cases of paroxysmal tachycardia or paroxysmal auricular fibrillation with coronary disease who

* Jonnesco, T.: Le sympathique cervico-thoracique, Masson et Cie, Paris, 1923.

do have real angina pectoris (a sort of status anginosus) during their rapid heart beating, but such patients are usually seriously crippled by angina pectoris on effort to start with. They are generally benefited by quinidine therapy but they live short lives after the beginning of such a history. The patient whose story I have recounted was not one of these.

There is a third point of interest. My patient for some years had temporary flashes of precordial pain when quiet, beginning at the time of her menopause. Such pain is almost always an excessive reaction of a nervously sensitive patient to an extrasystole. In such a case there is often tenderness on palpation of the precordium. Apparently in patients who have had painful reactions to paroxysmal tachycardia there may be developed a conditioned reflex to tachycardia that isn't even paroxysmal, that is, to a slight elevation of the heart rate of 20 or 30 or 40 beats, a sinoauricular tachycardia due to excitement or effort, so that even the rehearsal of the "sad story of illness" may precipitate one of these heart attacks, accompanied sometimes by tears.

A fourth point of importance is the patient's reaction to therapy. Quinidine was almost a specific, and it may very well be that some of the cases labeled angina pectoris who have been benefited by quinidine have had either painful sensations due to premature beats or paroxysmal tachycardia which have been controlled by the drug and which have been wrongly interpreted as angina pectoris due to coronary disease. In our case nitroglycerine was thought to have helped the transient pains but not the more prolonged heart attacks; it may conceivably have acted a little like exercise or atropine by raising the intrinsic heart rate and so abolishing extrasystoles. Digitalis, on the other hand, usually aggravates the uncomfortable symptoms produced by extrasystoles or paroxysmal tachycardia and may cause these disturbances of rhythm in the first place, as it did in myself experimentally twenty years ago.

The variations from the usual normal findings in the electrocardiogram and roentgen-ray picture in this patient of mine tended at first to cause further suspicion of heart disease. I shall mention them simply because they too are morals in this particular tale. Both the total inversion of Lead III and the reversed relationship of the measurements of the transverse and long diameters are unimportant findings in an individual who is fat, whose diaphragm is high, and whose heart lies horizontally, as in my case. Often in such cases the inclusion in the measurement of two or three centimeters of a triangular shadow of pericardial fat at the cardiac apex adds to the gross error.

The last point I would mention in my case is the possible relationship of the gall stone to the heart attacks. In the first place the stone did not cause the precordial distress although such a site of gall-bladder pain can occur, as I have recently experienced regretfully in a case wrongly diagnosed coronary thrombosis. When in my patient whose history I recounted above the gall stone did cause pain, that pain was upper abdominal and associated with vomiting. However, it is conceivable that the paroxysmal tachycardia

may have been a reflex manifestation of the gall stone or it may have been a reflex from something else if it was a reflex at all. At any rate it was not evidence of any rapidly progressive heart disease.

Before leaving the subject of heart pain I shall simply recount the 28 conditions mentioned by Dr. James Herrick, in a paper last year,* that he has himself found to have been confused with coronary thrombosis, which as we all know has recently been considerably overdiagnosed: paroxysmal angina pectoris, cardiac arrhythmias, cardiac neuroses, neurocirculatory asthenia, malingering, acute pericarditis, luetic aortitis with or without aneurysm, dissecting aortic aneurysm, pleurisy, pneumonia, carcinoma of bronchus or lung, massive collapse of the lung, pneumothorax, pulmonary embolism, herpes zoster, arthritis of costochondral articulation, shoulders, or spine, bursitis, gall stones, peptic ulcer, carcinoma of stomach or duodenum, acute gastritis, spastic colitis, diaphragmatic hernia, tabetic crisis, and impending diabetic coma.

2. **Dyspnea** is often misinterpreted. The common breathlessness of neurocirculatory asthenia in a nervously tired person or in one who is "soft" and physically unfit has been often treated as cardiac dyspnea with restriction in exercise and with digitalis therapy, when almost the opposite measures are indicated. A careful history should at once correct this error of interpretation and treatment, with the support of the finding on examination of no reason or evidence of myocardial weakness. The most common error in this respect is to be misled by the dyspnea of neurocirculatory asthenia when there is also present actual organic heart disease without failure. Long experience and good judgment are sometimes essential in the proper analysis of such a case. An extremely helpful clue when present is sighing respiration, which is never primarily due to heart disease. A patient who comes into your office and seats herself with a sigh saying "Well, here I am, doctor" reveals at least part of the diagnosis in the first few seconds of her interview.

Dyspnea of pulmonary origin is less commonly confused with cardiac dyspnea, but the error is often enough made to warrant much care in analysis. Chronic bronchitis with emphysema and weakness of the left ventricle with pulmonary vascular congestion and emphysema are the two conditions which in an elderly person, especially in the winter, are likely to be mistaken for each other. And sometimes they are actually superimposed. The history of respiratory infection, the presence of heart disease, roentgen-ray evidence, and the quick response to adequate digitalis therapy are the important clues; by their proper use the differential diagnosis is generally easy.

It should be observed that a chronic as well as an acute asthmatic state may be caused by congestion of the lungs secondary to heart disease. This is not widely appreciated.

One important error of interpretation that used to be made frequently but which is now uncommon is illustrated by the following case. A man 55

* Jr. Med. Soc. New Jersey, Oct., 1935, xxxii, 590.

years old is awakened at night by a severe pain in the epigastrium and lower anterior part of the chest. He gets up, takes hot water and soda bicarbonate, and belches gas. After a half hour without relief a doctor is called. He gives morphine subcutaneously with slight relief. A half hour later the patient vomits several times. Another hypodermic injection of morphine is given for the persistent pain which finally dies away after some twelve hours. The next evening the patient is wheezy and coughs a little. He prefers to sit up in bed. His lungs show scattered râles and emphysematous breathing. He may become definitely and even seriously asthmatic. His temperature is 101 degrees.

Both doctor and patient may be content with the one time "obvious" diagnosis of acute indigestion complicated by bronchitis or bronchopneumonia with asthma, but careful analysis and experience suggest the true diagnosis of coronary thrombosis with myocardial infarction followed by left ventricular dilatation with failure and acute pulmonary edema; the electrocardiogram will confirm the suspicion of coronary thrombosis in nearly every case. It is the morphine in such patients that may be wholly or at least in part responsible for the vomiting.

When there is marked mitral stenosis the most common symptom is dyspnea on effort, or in attacks (with or without asthma) or constantly. Such dyspnea is certainly to be ascribed to pulmonary vascular engorgement with too little room for air, as is evident by roentgen-ray examination and in fatal cases by autopsy finding of the marked engorgement of even the lung capillaries. But, granted all this, it is still the rule wrongly to attribute this dyspnea to heart, or rather myocardial, failure. To be sure, the dyspnea and pulmonary engorgement are due to the heart disease but they aren't due to myocardial failure. Rather the reverse. Actually the left ventricle is small, under no strain, not dilated, and not failing. The right ventricle is large and strong and also not failing, provided there is no increase in systemic venous pressure (as shown by normal neck veins, non-engorged liver, and no dependent edema). The answer is to be found in the disproportion between the strength and activity of the right ventricle and the narrow size of the mitral valve ostium. More blood is pumped into the lungs and left auricle in a given unit of time than can pass through the mitral valve—it is a mere matter of mechanics. It is thus obvious that digitalis will not help in such a case *unless it will reduce the heart rate* and thereby decrease the blood flow into the lungs. Fortunately in most cases of the sort digitalis does that very thing and hence is helpful. This is true in practically all cases of auricular fibrillation where the ventricular rate is at first rapid and uncontrolled. It is sometimes even true when the rhythm is normal, but far less frequently. At least the drug should always be tried. The slower the pulse rate in such cases the less the pulmonary congestion, and any measures besides digitalis that keep the heart from beating fast should be utilized.

There is one more important point concerning dyspnea that I shall mention. A good many individuals with heart disease and weakness are

troubled by insomnia. Very often this insomnia is frankly due to nervousness and very often to orthopnea secondary to pulmonary congestion, but there are borderline cases, and nervousness alone should not be blamed for the insomnia and treated as such, until the situation has been carefully analyzed. Digitalis and diuretic drugs may prove to be specific remedies for the insomnia in such patients.

3. **Palpitation** is due to the consciousness of forceful, rapid, or irregular heart action. It is never in itself a sign of heart disease and should never be prognosed and treated as such until the patient has been carefully studied. It may initiate a cardiac neurosis or even neurocirculatory asthenia unless properly handled at the outset. The most common condition associated with palpitation, that is more than the simple awareness of extrasystoles or short paroxysms of tachycardia, is neurocirculatory asthenia, of which it is frequently the chief symptom. Much has been written of the chance of confusing thyrotoxicosis, with its frequently disturbed heart rhythm and palpitation, with heart disease, but not so much has been said of confusing neurocirculatory asthenia with thyrotoxicosis. I shall recount briefly such a case.

An athletic young man, 20 years old, had a gruelling experience during the World War in 1918 and developed palpitation with a rather rapid pulse, nervousness, insomnia, exhaustion, and a precordial aching with a little dyspnea. When the war was over he rested and gradually recovered good health but three years later while studying hard in law he had a return of these same symptoms along with a feeling of tightness of the collar. Although worried about his health for a long time then, he did not consult a doctor because he was afraid that a serious diagnosis would be made. Finally after a year or two he did go to a physician who told him that he had an "athletic heart," and prescribed digitalis and bromide; the former drug did not help him, the latter did. Still not feeling well he consulted another doctor who made the diagnosis of thyrotoxicosis. Medical treatment of the condition seemed ineffective and finally partial thyroidectomy was done; at first he felt somewhat better but while still convalescent he had a year of heavy strain looking after his sick mother and later after his sick sister. Feeling poorly, with a return of all his old symptoms he consulted more doctors who suspected tuberculosis and advised treatment therefor which was carried out for a brief time. Then he returned to hard work with intense nervous strain and tried to save money on which to marry. He would return home exhausted every evening; but he continued to work hard and to worry about his work and his finances. His symptoms increased. He became panicky and finally consulted a doctor once more. Recurrent thyrotoxicosis was diagnosed and a second thyroidectomy was done four years after the first. Two months after the operation he felt somewhat improved and was married. His home life was very happy and his wife was sympathetic. His mental strain decreased and he no longer feared death, but he has never felt strong since this second operation. In a few years he began to feel nervously tense again; all his old symptoms recurred. Thyrotoxicosis was suspected once more but his basal metabolic rate was normal.

On examination last year I found this man, then 37 years old, to outward appearance in good health, very alert and breathing normally except for an occasional sigh. His reflexes were exaggerated. The thyroid gland was not enlarged; the neck showed an excellent scar. There was no abnormal pulse in the neck. The heart was normal in size, sounds, and rhythm. There were no murmurs. There was no evi-

dence of congestive failure. The pulse was regular at 120. The blood pressure was 145 systolic and 100 diastolic. Fluoroscopy showed a normally shaped, though unusually active, heart, a normal aorta, and normal lungs. Electrocardiography showed sinoauricular tachycardia with normal chest lead.

This man has improved in the past year on vigorous reassurance, regular exercise, ample rest, restricted work, omission of tea and coffee, small amounts of alcohol and tobacco, and the occasional use of bromides. It is obvious that his diagnosis is now, and quite probably always has been, neurocirculatory asthenia, whatever that is, and not thyrotoxicosis, tuberculosis, or heart disease. Cases somewhat like his are very common though not always so striking.

B. Signs. I shall now very briefly present a few cases illustrating common errors in the interpretation of cardiovascular signs.

1. **Cardiac Enlargement.** It is quite a common error for an over-active heart to be misjudged in size, especially by an inexperienced observer. The forceful apex impulse produces a widespread movement of the anterior chest wall which may be seen and felt several centimeters beyond the cardiac apex itself. If the outermost point of this impulse vibration is taken as the left edge of the heart, and especially if the measurement is made following the curve of the chest rather than tangentially from the midsternal line a gross and misleading error results. The maximal point of the apex impulse is to be taken as the position of the cardiac apex itself, using the much neglected and sometimes scorned but nevertheless valuable method of percussion for control, at least until a roentgen-ray examination is available.

It is a less common error to underestimate the heart size. There are to be sure still a few individuals who speak of normal heart size when the maximal apex impulse and left border of dullness are located in the left nipple line but fortunately their number is steadily decreasing. Rarely the nipple line may be near enough to the sternum to be the proper position for the left edge of a heart of normal size but almost always it is one to two centimeters too far to the left; the so-called midclavicular line should be used as a guide.

On a few occasions it is possible to misjudge the heart size grossly on hasty examination when a fairly forceful impulse is felt near or in the midclavicular line in patients with mitral valve disease whose hearts are very large and whose powerful right ventricles may displace the anterior chest wall while the true apex impulse is in or near the left anterior axillary line. I have recently made this error twice in the same patient whom I examined in April 1934 and again in December 1935—I had forgotten the first error. This was the case of a young woman with mitral stenosis and auricular fibrillation and a very large heart. It is of considerable interest and importance in such cases to observe that the characteristic diastolic murmur of mitral stenosis is often and in fact usually limited to the immediate vicinity of the true apex impulse in the axilla; if cardiac auscultation is not carried out to that region, the diagnosis of mitral stenosis may be missed. And again I would urge that careful percussion be also done in the third left interspace to detect marked increase in size of the infundibulum of the right

ventricle and prominence of the root of the pulmonary artery, particularly in cases with suspected mitral stenosis.

2. Now a few words about **heart murmurs.** I shall limit my remarks to two particular murmurs and I shall give two cases in illustration.

(*a*) A boy, eight years old, is seen in the third month of his first attack of rheumatic fever. He is still moderately ill with a slight elevation of temperature in the afternoon, occasional mild rheumatic pains and nose-bleeds, malaise, and slight leukocytosis. He had a pericardial friction rub for a few days a month ago. Observation shows a pale listless child lying in bed in no discomfort. No abnormalities are found on examination except for a regular rapid heart action of 120, a moderately enlarged heart, and blowing systolic and rumbling mid-diastolic murmurs at the cardiac apex. There are no thrills. There is no evidence of congestive failure in lungs, liver, neck, or dependent parts of the body. The diagnosis is made of subacute rheumatic infection, rheumatic heart disease, and mitral stenosis and regurgitation. He is thought to show early mitral valve disease with deformity, including stenosis.

An acute exacerbation of the rheumatic infection occurs and the boy dies four months after trouble started. Autopsy shows no deformity of any heart valve, but an enlarged dilated heart with myocardial rheumatic lesions (Aschoff bodies), small vegetations on the line of closure of the mitral valve, and acute fibrinous pericarditis.

Having been caught like this on a good many cases over a period of 10 years Dr. Bland, Dr. Jones, and I a few years ago began to suspect the truth and gradually assembled data which we published in the December 1935, number of the *American Heart Journal.* We believe that this paper is a very important one. The moral to the tale is that during a severe infection, especially rheumatic fever which attacks the myocardium, dilatation of the left ventricle may give rise to a mitral diastolic murmur (and in some cases even an accompanying thrill) which we used to think was pathognomonic of mitral stenosis, in the absence of free aortic regurgitation producing the so-called Austin Flint murmur. I believe that the murmur is due to the relative mitral stenosis (dilated left ventricular cavity and undeformed mitral valve) whether there is any aortic regurgitation or not. In the series of cases to which I am referring now particularly there was no aortic regurgitation. Hence when during acute or subacute rheumatic infection a mitral diastolic murmur is found to appear in the course of weeks or months it should be interpreted as I have done above and not considered to be evidence of real mitral stenosis; if it was heard before the infection or if there was a previous rheumatic infection some years earlier, then we are dealing with another matter and quite likely do have a mitral valve deformity with stenosis. It is important to remember that from this study close to two years must elapse after the beginning of a rheumatic infection of the heart before there is an appreciable stenosis of the mitral valve. Patients showing the mitral diastolic murmur due to left ventricular dilatation during acute or subacute rheumatism may die or they may recover—it is an important sign of myocardial infection and weakness. Those cases that recover may show a gradual transition in a period of years to true mitral stenosis, but sometimes they lose their murmurs altogether. When the mitral diastolic mur-

mur disappears with recovery we must not say that we are mistaken ever to have heard the murmur, nor can we say that valvular disease and deformity have been cured (as has sometimes been declared erroneously).

Parenthetically it may be added that other diseases besides acute rheumatic infection may cause temporary mitral diastolic murmurs as the result of left ventricular dilatation; this is especially the case in severe anemia due to any cause.

(*b*) A physician, 53 years old, consulted me in September 1926, because on a recent life insurance examination a systolic heart murmur had been found and he had been passed only with a higher age rating. He felt perfectly well but wanted me to tell him the significance of the murmur. He was a very healthy appearing, heavy man with good color and normal breathing. The only abnormalities were slight cardiac enlargement, a moderately loud blowing systolic murmur widely heard all over the precordium but maximal at the apex, without palpable thrill, and with a few premature beats. The blood pressure was 140 millimeters systolic and 90 diastolic. Electrocardiogram showed slight left axis deviation. I made a diagnosis of cardiac enlargement and mitral regurgitation, of unknown cause. He was advised to lose weight, to avoid fatigue, and to report for annual examinations. Lost to sight for nine years, he consulted us again last fall because of a history of attacks of acute pulmonary edema at night following a few months of rather poor health with dyspnea on effort after a grippe attack last spring. He was found in serious congestive failure. His heart was somewhat more enlarged than it was nine years earlier, the loud systolic murmur was much as before but more intense and as loud at the aortic valve area as at the apex, and now an aortic systolic thrill was easily felt. The aortic second sound was audible but less loud than an accentuated pulmonary second sound. The diagnosis of aortic stenosis was now evident with congestive failure therefrom.

The aortic stenosis was undoubtedly the cause of the widespread loud systolic murmur heard nine years before. The diagnosis was missed then, but now that we have had such experiences repeatedly we are becoming wiser and making the correct diagnosis earlier, before all the so-called classical signs appear. The etiology of the aortic stenosis in this case is in doubt as it is in many other patients. Rheumatic infection is obviously the cause in some and probably it is in a good many others; infection in middle aged men may be the cause in a few. Calcification often found is probably nearly always a complication, usually appearing late in advanced cases, and not itself the only cause of marked aortic stenosis. It should be possible to diagnose aortic stenosis by physical examination before there is enough calcification to show well by roentgen-ray study—the roentgen-ray diagnosis can be made only in advanced cases.

3. Finally, I shall have a word to say about errors in the interpretation of **congestion** including dropsy.

A married mill worker, 30 years old, mother of one child, was referred to me in January 1933, because of persistent dropsy. For two and one half years she had had gradually increasing anasarca, which had failed to yield to medical treatment consisting of rest, digitalis, and diuretic drugs. Several doctors had diagnosed heart disease and congestive failure. My examination revealed a slender woman with

marked edema of both legs extending to the hips and up to the waist with some fluid in the peritoneal and right pleural cavities, some engorgement of the neck veins with venous pressure of 16 centimeters, small regular pulse of 84 with blood pressure of 105 millimeters systolic and 70 diastolic, and heart normal in size with good sounds and no murmurs. Electrocardiogram showed low voltage of QRS and T-waves in all leads. Roentgen-ray examination revealed normal sized heart and aorta with little or no pulsation of right border but active pulsation of the left and upward displacement of the left leaf of the diaphragm with systole. These findings established the diagnosis of chronic constrictive pericarditis, and the operation of pericardial resection was carried out by Dr. Churchill in April 1933. A spontaneous diuresis began three days after the operation and within one month the dropsy had completely vanished with a loss of twenty and one-half pounds. She has been in excellent health ever since, having resumed work in the mill.

Here is an example of venous congestion due not to heart disease and failure but to the mechanical interference of a thick callous constricting pericardium. The same effect is produced by marked tricuspid stenosis in rare cases. Comparably, as I have already said, when there is pulmonary vascular congestion in marked mitral stenosis, it is not primarily myocardial failure that is responsible, but the mechanical influence of the valvular defect. This viewpoint is of great importance in the proper understanding and treatment of vascular congestion not due to myocardial failure.

I have herewith presented a number of cardiovascular symptoms and signs that are likely to be misinterpreted. Through our diagnostic errors in the past, caused by such misinterpretation, important advances have been made. We should search diligently for more errors in the future for there is still a great deal for us to learn therefrom.

THE INITIAL VENTRICULAR COMPLEX OF THE ELECTROCARDIOGRAM IN CORONARY THROMBOSIS *

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THE changes in the final ventricular complex, the T-wave, and in the S–T segment of the electrocardiogram in coronary thrombosis have been extensively studied, both experimentally and clinically, since the early works of Herrick,[1] Smith,[2] and Pardee.[3] As a result, it has been generally accepted that characteristic changes do occur in the majority of the cases, following an attack of coronary thrombosis.

In contrast, the changes in the initial ventricular complex have, up to recent years, received much less attention. Smith [2] and Wearn [4] observed that in coronary thrombosis the initial ventricular complex may not rarely be of a very small amplitude. The former observed such a reduction of the amplitude following coronary ligation in animals. Oppenheimer and Rothschild [5] found arborization block in a number of their cases of coronary thrombosis that were studied postmortem. Various grades of intraventricular conduction disturbances have been reported to have appeared following coronary thrombosis.

That Q_3 may become prominent in myocardial infarction was first observed by Pardee,[6] and later by Wilson,[7] Parkinson and Bedford,[8] and by Levine.[9] Fenichel and Kugel [10] suggested that a large Q_3 in coronary thrombosis was probably due to involvement of the posterior portion of the ventricular septum, and that large Q deflections in other leads may have a similar clinical significance.

On the other hand, many articles [11, 12, 13, 14] have appeared showing that a large Q_3 may also be encountered in such conditions as coronary sclerosis, hypertension, obesity, pregnancy, rheumatic heart disease (without right axis deviation), and not rarely as a variation of the normal electrocardiogram. Wilson [15] and his associates recently described certain changes in the initial deflection of the ventricular complex in association with coronary thrombosis. They classified these changes as belonging to Q_1 and Q_3 groups. The former was most frequently observed in association with the T_1 type of electrocardiogram, and the latter with the T_3 type, as classified by Parkinson and Bedford.[8]

The Q_1 group is characterized by "the presence of a conspicuous and, in most instances, rather broad Q in Lead I; the absence of Q in Leads II and III; the small amplitude of the largest of the initial deflections in Lead I; and the presence of a conspicuous S in Leads II and III. In some instances

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one or more of these characteristics may be absent or poorly developed. Nevertheless, all of these curves display a family resemblance."

The Q_3 group is characterized by "the absence of Q in Lead I; the presence of a conspicuous Q in Leads II and III; and relatively small amplitude of the initial ventricular deflection in Lead II." Here, too, the authors stress the fact that not all curves show all the characteristics mentioned. They add: "Curves in which Q is absent in Lead II, as well as in Lead I, and in which T is inverted in Lead III only, are not infrequent in myocardial infarction; they are not rare, however, in young individuals in whom there is no reason to suspect cardiac disease."

The absence of characteristic changes in the S–T segments or in the T-waves in some of the authors' curves is attributed by them to the long interval that elapsed between the occurrence of the infarction and the recording of the tracings.

Winternitz [16] described changes in the initial ventricular complex of the electrocardiogram in coronary thrombosis. His first group is not unlike the Q_1 group of Wilson.[15] His second group is characterized by negativity of the principal deflections in all leads. The amplitude is low and the main deflection may be Q or S. His third group is typified by intraventricular conduction disturbance, resembling arborization block.

Barnes [17] studied a group of cases and he found that coronary thrombosis is frequently followed by electrocardiographic changes that conform to the Q and T patterns. He concluded that the combined consideration of the changes in the initial and in the final ventricular complex yields more information regarding coronary thrombosis than does the study of either change alone.

Durant [18] studied 74 cases of coronary thrombosis, and he found that 38 cases (51.3 per cent) showed changes in the initial ventricular complex of either Q_1 or Q_3 types. He concluded that the relative permanence of these changes greatly enhances their value in the recognition of old myocardial infarcts.

Since various conditions, such as rheumatic fever, pericarditis, coronary sclerosis, anoxemia, large fatigued hearts, digitalis, uremia, pneumonia, etc., are known to produce changes in the S–T segment and in the T-wave very much akin to those seen in coronary thrombosis, the uncovering, by the authors mentioned above, of changes in the initial ventricular complex that may be produced by the latter condition should be of great value.

Material Studied

One hundred and eight electrocardiograms of patients with coronary thrombosis were reviewed. The diagnoses were based on good clinical evidence. Service cases had the opinions of the attending staff, and private cases had frequently the opinion of a cardiac consultant, although characteristic changes in the electrocardiogram, when they occurred, were taken

into consideration in reaching a decision. In most instances the patient was seen and an electrocardiogram taken some hours or days after the onset of symptoms. Only very few patients were seen weeks after, unless they experienced a new attack before completely recovering from the first. Very frequently the tracing was repeated in a few days, less frequently was a third one taken, and in practically none was a serial study made. Of the 34 patients that died, eight were studied postmortem.

Eleven electrocardiograms showed no changes of any kind. Forty-five cases displayed various changes in the S–T interval and in the T-wave significant of coronary thrombosis, but had no changes in the initial ventricular deflection. Fifty-one cases exhibited Q patterns associated with T-changes. There was one case which showed a marked left axis deviation with a good-sized Q_1, without changes, recent or old, in the final ventricular complex. She died soon after admission; no autopsy was obtained. Twelve cases showed extremely low Q–R–S complexes.

Curves of the Q_1 Group

Using the criteria of Wilson [15] and his associates, we classified 19 cases as belonging to the Q_1 group. Almost all of these had in association changes of the T_1 type. The six curves in figure 1 represent the typical changes and the variations of this group, showing that the family resemblance prevails.[15]

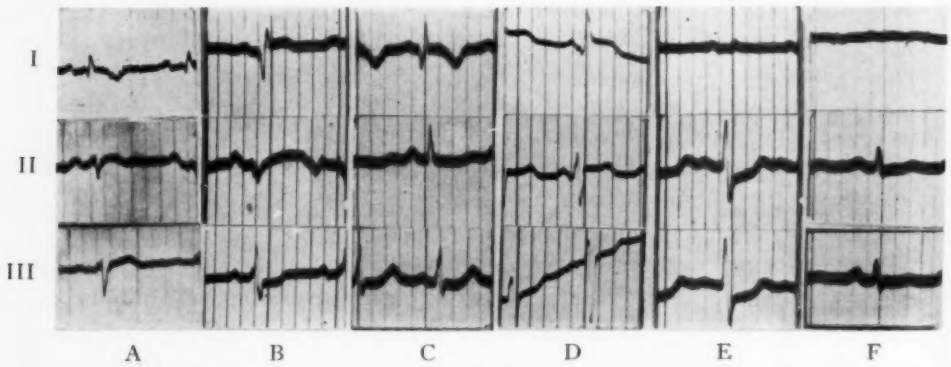

Fig. 1. Electrocardiograms of six patients displaying initial ventricular deflections of the Q_1 type.

Figure 1A typifies this group. There is a conspicuous Q in Lead I. In Leads II and III the first ventricular deflection is upward and is followed by a deep S-wave. The initial deflections are small in Lead I. T_1 is sharply inverted, and the S–T_2 and S–T_3 intervals are elevated and rounded. The patient was a man 40 years old who had a typical attack three weeks before the tracing was taken. He recovered.

Curve 1B was taken three days after the attack in a man 56 years old,

who nine months previously was seen with a severe attack of coronary thrombosis. He survived the second attack, dying suddenly two months later. This curve is similar in general outline to that shown above, although it differs from the latter in some detail; the amplitudes of the initial deflections in Lead I are comparatively large; S_3 is comparatively small; and S_2 is widened and rather inconspicuous. $S–T_1$ is elevated, $S–T_2$ is elevated and rounded, giving a monophasic curve, and $S–T_3$ is depressed. It is possible in this case that the somewhat atypical changes in the initial ventricular complex may be due to the ancient infarction. That the Q may persist for such a length of time following the attack was stressed by Wilson.[15]

Tracing 1C is also quite different in detail from the typical. While Q_1 is prominent, R_1 is quite large. S_2 is lacking and S_3 is small. T_1 is sharply inverted, and $S–T_2$ interval is slightly depressed. This tracing was taken seven weeks after the attack in a man 57 years old. He recovered. The time interval, here too, is probably responsible for the variation, for the tracing is more characteristic of an old infarct than of a fresh one.

Figure 1D is that of a man 59 years old, taken four days after the onset of an attack, and one day before his death. Except for a large R_1 it is typical of the group under consideration. There is also intraventricular conduction disturbance. The changes in the S–T intervals are highly significant of coronary thrombosis in the acute phase.

Curve 1E represents still another variation of this family group. The very low amplitude of the initial ventricular deflections and the conspicuous S_2 and S_3 qualify this electrocardiogram for the Q_1 group, in spite of the absence of Q_1. The absence of the latter is probably due to the low voltage in Lead I. The S–T intervals are not markedly altered, probably due to the time interval since the attack, which happened three weeks previously. This was a woman 59 years old, dying the day after the tracing was taken. This curve is similar to that shown by Wilson [15] (see his figure 8) which is of a man 44 years old, with coronary thrombosis. Autopsy showed occlusion of the anterior descending branch of the left coronary artery. The infarcts invaded the anterior and lateral walls of the left ventricle.

Tracing 1F is also slightly different from the typical in this group. The very small Q in Lead I, the small S in Lead III and the inconspicuous S in Lead II are all probably due to the low voltage. $S–T_1$ is altered, while the final complexes in the other leads show no conspicuous changes. It is a tracing of a man of 60, one week after the onset. He recovered.

Except for the duration of Q_1 and its relative amplitude in comparison with the succeeding upstroke, the initial ventricular deflections of some of the curves typical of this group are very similar to those of left axis deviation, due to preponderate hypertrophy of the left ventricle (figures 1A and 1D). It is also possible that left ventricular hypertrophy, which is common in patients of the class subject to coronary thrombosis, may have played a part in determining the form of the initial ventricular deflections, especially large S_2 and S_3. Wilson,[15] however, shows that myocardial infarction may

produce such curves. He cites a case (see his figure 4) having an electrocardiogram taken before and after the attack of coronary thrombosis. The latter showed the development of large S_2 and S_3, and a very small initial deflection in Lead I. Q_1 is not definite but suggestive. He cites another similar case (see his figure 5), thus proving that infarction may produce such changes in the form of the initial ventricular complexes.

Curves of the Q_3 Group

Twenty records were classified into the Q_3 group, all of which were associated with T_3 type changes. The six curves in figure 2 are representatives of this class.

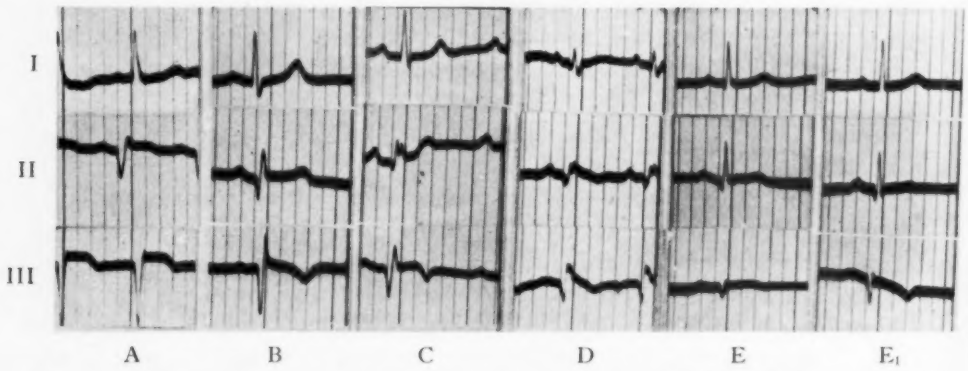

Fig. 2. Electrocardiograms of five patients showing initial ventricular deflections of the Q_3 type. Tracings E and E_1 are of one patient, taken three days apart.

Figure 2A is typical of this type of curve. The characteristic features are: absence of Q in Lead I, the presence of a conspicuous Q in Leads II and III, and the relatively small amplitude of the initial ventricular deflections in Lead II. In Lead III, Q is often the largest and, at times, the only initial deflection. It is a tracing of a man of 58 years, taken two days after the attack, from which he survived. There are definite S–T and T changes of the T_3 type.

Curve 2B is that of a man 43 years old, taken two days after the attack, from which he recovered. The curve is similar to the previous one, with the exception of a conspicuous R in Leads II and III. The changes in the final ventricular complex are those of type T_3.

Tracing 2C is of a man 63 years old, one day after the attack. The Q in Lead II is not as prominent as in the previous curves, but the amplitude of the initial ventricular deflections is more typical. The R in Lead II is quite notched. The S–T and T changes are characteristic of the T_3 type. The patient improved, but continued to show marked myocardial insufficiency.

Figure 2D is a typical tracing of the group under consideration. It is of a man 67 years old, four days after the attack and one day before death.

There is also evidence of intraventricular conduction disturbance, and the changes in the final complex are those of an acute phase of infarction.

Curves 2E and 2F are of one patient, a man 48 years old. The former was taken two days following the attack. This curve is not typical of the class under discussion. The Q_2 is small, R_2 quite large, and Q_3 very small. The S–T intervals show only slight changes. The latter curve was taken three days later and five days following the attack; Q_3 has become prominent, T_3 more inverted, and T_2 flattened. The initial ventricular complexes in the other leads did not change. This curve is an example of the appearance of a large Q_3 and inverted T_3 following coronary thrombosis.

Curves of this description are not rare in coronary thrombosis.[6, 7, 8, 9] There were 12 other such curves in our 108 records. However, as mentioned above, they may also be seen in conditions other than coronary thrombosis.[11, 12, 13, 14, 15]

Persistence of QRS Changes

Since our cases were seen mostly days after the infarction, the persistence of the changes in the initial ventricular complexes could not be studied. Those cases seen by us weeks after the attack and a few months after, were again in the throes of a new attack on admission, thus precluding any conclusions. Wilson [15] and his associates express the opinion that the changes in the initial ventricular complex of the types described are often more persistent than the characteristic changes in the final deflection of the ventricular complex, and that they may be helpful in recognizing an old myocardial infarction. They cite a case in whom Q_2 and Q_3 were present five and one-half months after the infarction, while the T reverted to normal long before.

Wallace [19] cites a case showing persistent Q_2 and Q_3 almost one year after the acute attack of coronary thrombosis and months after the changes in the final ventricular complex had disappeared.

Correlation with Postmortem Findings

Wilson [15] and his associates, in discussing the correlation of the Q_1 and Q_3 type of electrocardiogram with the location of the infarct, concluded that while infarction in the anterior wall of the left ventricle and the adjacent septum was generally associated with ventricular complexes of the Q_1–T_1 type, it may be accompanied by curves of the Q_3–T_3 type, or possibly by no definite electrocardiographic changes of any kind. They also found instances both in their own series and in those reported in the literature, where curves of the Q_1–T_1 type were produced by infarction of the posterior wall of the left ventricle.

Barnes,[20] in correlating the changes in the initial ventricular deflections with the site of the myocardial infarct, concludes that tracings typical of the Q_1–T_1 group are found to be associated with infarction of the anterior wall of the left ventricle and the adjacent septum. Infarction of the posterior

wall of the left ventricle and the adjacent septum is accompanied by curves of the Q_3–T_3 group.

Eight cases of our series were autopsied. The location of the infarcts and the changes in the coronary arteries were carefully studied by Dr. I. Davidsohn, with the following results.

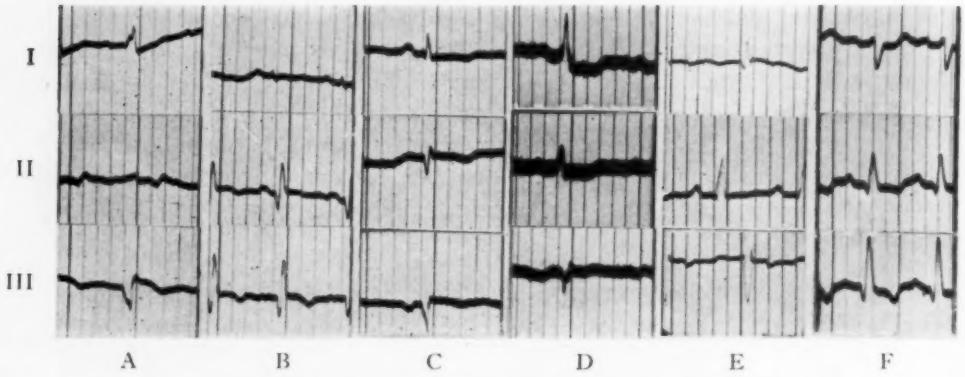

FIG. 3. Electrocardiograms of six patients that were studied postmortem.

Figure 3A is that of a man 68 years old, who died one week after the attack. It belongs to the Q_3–T_3 group. The opening of the right coronary artery was completely occluded by a thrombus. The left coronary artery showed a moderate degree of sclerosis. Acute myomalacia of the posterior wall of the left ventricle and the posterior half of the septum was found. There were pericardial adhesions posteriorly.

Figure 3B is that of a woman 69 years old, who died three weeks after the attack. The tracing was taken one week after the onset, and it belongs to the Q_3–T_3 type. There was a complete occlusion of the left circumflex artery, with myomalacia of the posterior wall of the left ventricle and, to a lesser degree, of the posterior half of the septum.

Figure 3C. This was a man 45 years old. The tracing belongs to the Q_3 group. The first attack came six weeks prior, and the second two days before the tracing was taken. He died two days later. There was occlusion of the entire descending branch of the left coronary artery, with an aneurysm of the left ventricle at the apex. There was also recent thrombosis of the right coronary artery near its mouth, with acute myomalacia of the posterior wall of the left ventricle, right ventricle, and the posterior half of the septum. T_1 is diphasic, T_2 is inverted, and S–T_3 is elevated. The changes in the initial ventricular complex fit in with posterior infarction, while the changes in T_1 and T_2 may be remnants of the anterior infarction.

Figure 3D is a tracing of a man 57 years old, one week after the attack. He gave no history of any previous attacks. There is only Q_3 present, which is slurred and atypical. There is depression of all the S–T segments. He died two weeks later. There was an obliterating thrombosis of the

anterior descending branch of the left coronary artery, with an aneurysm of the left ventricle at the apex. More recent thrombosis of the right coronary artery near its orifice with acute myomalacia of the posterior wall of the left ventricle was also present. The more recent infarction possibly is responsible for the Q_3 (Fenichel and Kugel [10]), while the diphasic T-waves may be a vestige of the older damage.

Figure 3E. A woman 62 years old. The tracing was taken two weeks after the attack. She died three weeks later. There is a small Q_1 and a deep Q_3. The changes in the final ventricular complex are not readily discernible. There was a thrombosis of the left descending coronary artery and of the circumflex branch, also acute myomalacia of the anterior wall of the ventricle, and, to a lesser extent, on the posterior wall.

Figure 3F is a tracing of a woman 50 years old. She had severe nocturnal dyspnea with collapse two weeks before the tracing was recorded. Death occurred three weeks after the onset. The electrocardiogram shows right axis deviation with conspicuous Q_3; T_2 and T_3 are inverted. There was a thrombosis of the first part of the anterior descending branch and of the circumflex branch of the left coronary artery. There was also an occlusion of the right coronary artery 3 cm. from its origin. Fairly recent myomalacia of the apex, the adjacent septum, the posterior wall of the left ventricle, and the posterior half of the septum resulted.

Figure 4D is a tracing of a man 60 years old, taken three days after the attack. He died three weeks later. The tracing does not belong to either of the groups under consideration. The changes in the final ventricular complex are significant, but not typical of any particular type. There was thrombosis of the circumflex branch of the left coronary artery, with acute myomalacia of the posterior wall of the left ventricle.

Figure 4E. A man 61 years old. The tracing was taken three days after the attack and two days before death. Except for the low amplitude and slurring, there are no significant changes in the initial ventricular complex. The T changes are of the T_3 type. There was a thrombosis of the circumflex branch of the left coronary artery, atheromatous changes in the descending branch of the left coronary artery, and also in the right coronary artery. Early myomalacia of the posterior wall of the left ventricle resulted.

Hence, four cases showing infarction of the posterior wall of the left ventricle had tracings of the Q_3–T_3 type. In two cases having both anterior and posterior infarctions the electrocardiograms did not conform to any type. However, the right axis deviation in one of them (figure 3F) is rather significant. One case of posterior infarction failed to show changes conforming to either the Q_1 or Q_3 type. Finally, the last case of posterior infarction showed typical T changes; the initial ventricular complex was of low amplitude and markedly slurred, but without any Q waves.

Other Changes in the Initial Ventricular Complex

There were 12 cases in our series showing extremely low initial ventricular complexes. These changes, helpful in the diagnosis of coronary thrombosis, were described previously.[4, 5, 16] The first three tracings in figure 4 represent such changes.

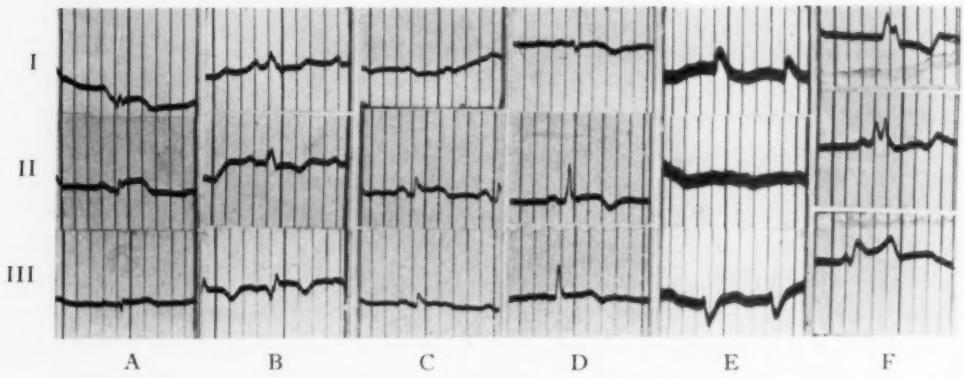

Fig. 4. Electrocardiograms of six patients. A, B, C, and D display low amplitude of the QRS deflections. D and E were studied postmortem, and F shows bundle branch block.

Figure 4A is that of a man 42 years old, taken three days after an attack. The S–T and T changes are not unlike those described by Barnes [21] as occurring in coronary thrombosis complicated by pericarditis. The patient recovered.

Figure 4B. This is the tracing of a man 67 years old, taken three weeks following an attack, and three days before death. The curve conforms to the Q_3–T_3 type.

Figure 4C is that of a man 60 years old, taken six days after the attack. He improved.

Figure 4F shows bundle branch block of the common variety. We had six such tracings in our series. This patient was 69 years old. The tracing was taken 10 days following the attack, and one week before death. Such changes in conduction are helpful in the diagnosis of coronary thrombosis.[5, 15]

Summary

One hundred and eight electrocardiograms of patients with coronary thrombosis were studied with particular reference to the changes in the initial ventricular complexes.

Eleven tracings showed no changes in either the initial or the final ventricular complexes.

Forty-five cases showed changes in the final ventricular complex (S–T and T-waves) only.

Fifty-one records (47.22 per cent) displayed conspicuous Q-waves in association with characteristic changes in the S–T segments and T-waves.

Nineteen of these, belonging to the Q_1 group and almost always associated with the final ventricular deflection of the T_1 type, displayed often a conspicuous Q-wave in Lead I, while the other Q–R–S deflections in this lead were small. In Leads II and III, the first deflection of the ventricular complex is upward and is often followed by a large S deflection. However, Q_1 may be very large and S_2 and S_3 may be small or absent.

Twenty tracings of the 51 were classified into the Q_3 group and were accompanied by the final ventricular deflection of the T_3 type. The characteristics are usually a large Q-wave in Leads II and III, but no Q in Lead I. There is frequently a relatively small amplitude of the initial ventricular deflections in Lead II.

There were twelve curves showing Q_3–T_3 only. In one case this finding was inconspicuous two days after the attack, only to become prominent three days later.

Since various other conditions may be associated with changes in the S–T segments and T-waves, the presence also of changes in the initial ventricular complex is of additional value in the diagnosis of coronary thrombosis.

Changes in the initial ventricular complex without accompanying changes in the final ventricular complex are rare in acute coronary thrombosis. Such a curve would speak, instead, for an old infarction.

Most of the cases that had posterior infarctions showed tracings of the Q_3–T_3 type, while the rest, either having multiple infarctions or a single posterior one, displayed curves that did not conform to either Q_1 or Q_3 groups. The number of autopsies being small, no definite conclusions can be drawn.

Other changes in the initial ventricular complex, such as marked reduction in amplitude, or the development of intraventricular conduction disturbances, may occur in coronary thrombosis.

REFERENCES

1. Herrick, J. B.: Thrombosis of the coronary arteries, Jr. Am. Med. Assoc., 1919, lxxii, 387.
2. Smith, F. M.: Ligation of coronary arteries with electrocardiographic studies, Arch. Int. Med., 1918, xxii, 8.
3. Pardee, H. E. B.: An electrocardiographic sign of coronary artery obstruction, Arch. Int. Med., 1920, xxvi, 244.
4. Wearn, J. T.: Thrombosis of coronary arteries, Am. Jr. Med. Sci., 1923, clxv, 250.
5. Oppenheimer and Rothschild: Electrocardiographic changes associated with myocardial involvement, Jr. Am. Med. Assoc., 1917, lxix, 429.
6. Pardee, H. E. B.: Clinical aspects of the electrocardiogram, First Ed., 1924, Paul B. Hoeber, Inc., N. Y., p. 82.
7. Wilson, W. J.: Cardiac clinic with electrocardiographic demonstrations, Ann. Clin. Med., 1926, v, 238.
8. Parkinson, J., and Bedford, D. E.: Successive changes in the electrocardiogram after cardiac infarction, Heart, 1928, xiv, 195.

9. LEVINE, S. A.: Coronary thrombosis—its various clinical features, Medicine, 1929, viii, 245.
10. FENICHEL, N. M., and KUGEL, V. H.: The large Q-wave in the electrocardiogram, a correlation with pathological observation, Am. Heart Jr., 1931, vii, 234.
11. STRAUSS, S., and FELDMAN, L.: The significance of the large Q in Lead III, Am. Jr. Med. Sci., 1933, lxxv, 87.
12. EDEIKEN and WOLFERTH: Incidence and significance of deep Q in Lead III, Am. Heart Jr., 1932, vii, 695.
13. ZISKIN, T.: Clinical significance of the electrocardiogram with large Q in Lead III, Arch. Int. Med., 1932, l, 435.
14. FELDMAN, L., and HILL, H.: The electrocardiogram of the normal heart in pregnancy, Am. Heart Jr., 1934, x, 110.
15. WILSON, F. N., MACLEOD, A. G., BARKER, P. S., JOHNSTON, F. D., and KLOSTERMAN, L. L.: The electrocardiogram in myocardial infarction with particular reference to the initial deflection of the ventricular complex, Heart, 1933, xvi, 155.
16. WINTERNITZ, M.: The initial complex of the electrocardiogram after infarction of the human heart, Am. Heart Jr., 1934, ix, 616.
17. BARNES, A. R.: Q and T types of electrocardiograms; their comparative and complementary value in indicating occurrence of acute myocardial infarction, Am. Heart Jr., 1934, ix, 722.
18. DURANT, T. M.: The initial ventricular deflection of the electrocardiogram in coronary disease, Am. Jr. Med. Sci., 1934, clxxxviii, 225.
19. WALLACE, A. W.: The Q-wave in the electrocardiogram, Am. Jr. Med. Sci., 1934, clxxxviii, 498.
20. BARNES, A. R.: Correlation of initial ventricular complex with situation of acute myocardial infarction, Am. Heart Jr., 1934, ix, 728.
21. BARNES, A. R.: Electrocardiographic pattern observed, following coronary occlusion, complicated by pericarditis, Am. Heart Jr., 1934, ix, 734.

LATE RECRUDESCENCE IN ENCEPHALITIS LETHARGICA WITH SUCCESSION OF NEW MANIFESTATIONS AT INTERVALS OF YEARS; THE PROBLEM OF PROGNOSIS *

By Alfred Gordon, F.A.C.P., *Philadelphia, Pennsylvania*

It is pretty well established that the virus of encephalitis lethargica may invade any area of the central nervous system but has a special affinity for the striatal region in the mid-brain. The Parkinsonian symptom-group is the usual clinical expression of this localization. As to the so-called sequelae, the literature shows a multiplicity of phenomena. The sensory system, the special sense organs, the motor system, the vegetative nervous system, the psychic functions—all may show morbid alterations. Some of these various manifestations are rare or very rare, while others are common. Hyperkinetic phenomena are the most frequent. Since, in some cases, the postencephalitic sequelae are chronologically not far distant from the original malady, and since usually when they do occur, they remain fixed, it might seem a logical deduction that the pathological substratum, which is directly responsible, is fixed and shows no tendency to extension and further involvement. On the other hand there are cases in which aggravation of the preëxisting symptoms occurs and also the appearance of new manifestations. Such observations, of course, can only signify a progressive and extensive development of the original lesions, due in all probability to the persistence of the encephalitic virus in the nervous tissue. The clinical histories of many such cases indicate that the virus may remain active in the nervous tissue for a considerable time, that it is capable of causing new anatomical lesions and extensions of preëxisting ones. They also indicate that there is no certainty as to whether the virus is ever completely eliminated, and if its elimination is possible, within what period of time it may be accomplished. It is uncertain also, should the virus be eliminated, whether the lesions can regress, and to what extent and with how much consequent amelioration of the clinical manifestations. Our present therapeutic resources do not include any method of neutralizing the virus in order to obtain a regression of the anatomical lesions and consequently a modification in the course of the syndrome. The postencephalitic manifestations should not be considered merely as sequelae, but as forms of a genuine chronic evolution in the presence of a virus which is still active.

The present contribution has for object to put on record additional data demonstrating the grave possibility that the apparent subsidence of an encephalitic invasion does not necessarily indicate a finished process, and that

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Patients presented before the Philadelphia Neurological Society.

the virus may exist in a latent state even for many years, during which the clinical manifestations remain unaltered and fixed. Recrudescences may develop, not only after the acute state, but also many years later; and new phenomena may appear in the domain of extrapyramidal, pyramidal, bulbar and cerebellar domains, or at any level of the central nervous system. The succession of pathological manifestations in the same individual at intervals of years demonstrates the fact that the so-called sequelae are not of evolutional character, but late and definite reactivations of the original infectious process, especially characteristic of lethargic encephalitis. These observations have a very considerable and serious bearing on the prognosis in this grave affection. They prove that it would be erroneous to assume a final position as to the course of lethargic encephalitis even after the Parkinsonian syndrome became definite. Besides the main object of this presentation, namely to suggest the importance of a reserved prognosis, attention is also called to some new and unusual features which have not yet been recorded in the literature as very late occurrences in lethargic encephalitis of long standing.

Case Reports

Case 1. M. P., a newspaper dealer, 35 years old, 15 years earlier had a condition characterized by sudden onset, somnolence, fever, and double vision. He was bedridden for four weeks. He then presented the attitude, general fixation, facies and fine tremor of the hands and lips, characteristic of the Parkinsonian syndrome following an acute attack of encephalitis lethargica. The condition remained unaltered for six years, when he developed the oculogyric manifestations from which he is still suffering. The eyes roll up suddenly and may remain in that position for between one and 10 hours. An emotional upset may precipitate an attack, but emotion is not the exclusive exciting factor. Physical fatigue may do likewise. On the other hand the upward deviation of the eyes may occur even after a good rest or early in the morning, before he commences to work. Sometimes the attack occurs while the patient is in his conveyance, distributing papers. The patient is absolutely unable to overcome this condition. All possible efforts on his part to bring the eyes down are futile. In his work he is obliged to be accompanied by someone as he is unable to continue his work and cannot walk by himself while the eyes are in the upward position. Seven months ago, that is over 14 years after the acute attack, he developed another additional disorder. Almost at every meal, while masticating his food, there occurs a sudden rigidity and immobility of the tongue, and the patient is unable to roll the food from side to side. This may last as long as five or ten minutes. These paroxysms have been quite frequent of late. Three months ago he developed another additional symptom, namely sudden closure of his eyes which, like the other symptom, may set in without warning. Any effort on his part to reopen the eyes is useless. This manifestation lasts a shorter time than the upward movements of the eyes, but, like the latter, it equally incapacitates him and interrupts his work.

The previous medical history of the patient is essentially negative. Lues is improbable since the Wassermann reaction of blood and spinal fluid is negative. Urinalysis is negative. Eye grounds are intact. There is no organic involvement of the ocular muscles. The circulatory system is normal. The reflexes, sensations, pupillary reactions are all intact. There are no pathological reflexes.

To sum up, we are dealing with a typical case of Parkinsonian syndrome subsequent to an attack of lethargic encephalitis 15 years earlier. Since

then, at different periods up to the present and at intervals of years between each other, the patient has developed three different phenomena, namely: six years after the onset of encephalitis, the oculogyric phenomena; five years still later, the attacks of rigidity and immobility of the tongue; and much later (about three months ago) attacks of uncontrollable closure of the eyelids with hypertonicity of the orbicularis palpebrarum muscles.

Case 2. S. S., girl, 20 years of age, seven years ago developed a typical attack of lethargic encephalitis (somnolence and fever). Shortly afterwards she observed a stiffness of the jaw and later an impediment of speech. The condition progressed for a time and then remained stationary. The speech disorder presented certain unusual features. Briefly, while speaking the tongue protrudes between the teeth, rolls, curls and moves to the right side; at the same time two deep furrows appear on both sides of her mouth. (For details of this unusual postencephalitic manifestation, the reader is referred to the ANNALS OF INTERNAL MEDICINE, 1933, vi, 895.) There is no evidence of aphasia, paraphasia, or anarthria. Because of the dysfunction of the tongue, the food remains in the mouth a long while, and there is also pronounced salivation. The palate and pharynx are intact. Simultaneously with the speech-disorder appeared myoclonic contractions of the muscles of the left hand, so that the fingers would flex and extend alternately. Somewhat later a tremor was observed in the same hand. During a period of four years this speech manifestation and the tremor of the left hand were the only postencephalitic sequelae. At the end of the fourth year the patient began to observe a gradually oncoming weakness of the right upper extremity. At that time both knee-jerks were increased, but there were no other pathological reflexes. One year ago, that is six years after the acute attack, for the first time she noticed a tendency to turn her head to the left. This condition gradually increased in frequency and intensity so that, at present, a typical spasmodic torticollis is established. The former paretic condition of the right arm has greatly increased within one year, so that she is compelled to use her left hand almost exclusively. Moreover, the right leg, in addition to the increased knee-jerk, presents now an extensor plantar reflex, a condition which was not present two years ago. A general somatic examination is essentially negative. Blood, spinal fluid, urine, show no special disorder worth mentioning. The mental state is normal.

To sum up, the following course of events has been observed in a period of seven years. At first a typical picture of encephalitis lethargica. Shortly after the acute period, there developed an unusual speech disorder which persists at present, also myoclonia and tremor of the left hand. The next abnormal symptom (four years later) was a paretic state of the right arm which progressively increased. Next, in the chronological disorder (in the fifth year), was the extensor plantar reflex on the right side, and finally a progressive spasmodic torticollis became established. The clinical symptoms, therefore, indicate an involvement of the extrapyramidal and pyramidal systems. The speech disorder, with particular disturbance of the function of the tongue in the act of speaking, may be the result of a nuclear involvement in the medulla or rather of an interruption in the structural connection of the striatum with the important bulbar segments of the central nervous system.

Hypertonia or dystonia and hyperkinesia are met with frequently in the postencephalitic period. The muscular phenomena may be generalized or

limited to circumscribed areas. They may be due to an irregular muscular function confined to the peripheral agencies. An improper and abnormal use of the many small muscles which enter into the formation of syllables and words in speech, and therefore in the enunciation of words, may be the cause of the speech disorder. The hyperkinesia in the form of the torticollis is another clinical evidence of a new invasion of the striatal connections.

In this case, as in the first, we observed several encephalitic sequelae, developing at very long intervals between each other, demonstrating the existence of latent or silent periods of years' duration after the acute attack of infection. Therefore a final fixed stage in the disease under discussion is not admissible.

Conclusion

Two cases are reported which are instructive from the standpoint of prognosis in encephalitis lethargica. Even years after the onset of this disease recrudescences may occur attacking any part of the central nervous system. The so-called sequelae are an indication of chronicity of the pathological processes and persistence of the virus.

CASE REPORTS

RENAL DWARFISM; A CASE REPORT *

By J. F. Roberts, M.D., *Toronto, Canada*

The relationship between chronic interstitial nephritis in childhood and the occurrence of infantilism, late rickets, and dwarfism as sequelae, was first clearly defined by Fletcher [1] in 1911. Thirty years previously Lucas [2] had noted the frequent association of albuminuria with late rickets but had regarded the albuminuria as functional. Renal dwarfism, however, has only been recognized as a definite clinical entity since 1920, when Barber [3] introduced the name, and defined it as "a condition of stunted development, associated with bone deformities of the 'late' rickets type, due to an insidious chronic interstitial nephritis of obscure etiology." The terms, renal dwarfism, renal infantilism, and renal rickets have been variously used for this group of cases, depending on whether dwarfism, infantilism or rickets was the predominating clinical feature. At present there are about one hundred examples of this condition recorded.

Attention has recently been drawn, by Ellis and Evans,[4] to the importance and frequency of other abnormalities occurring in the urinary tract in this condition, namely, hypertrophy of bladder and dilatation of ureters and kidney pelves, without any malformation or lesion to account for the obvious obstruction. In their report of 20 cases which came to postmortem, 14 showed these changes, but no organic lesion was found, and the author suggested a disorder of the neuro-muscular mechanism controlling the urethro-vesical sphincter, as the responsible factor.

More recently Ellis [5] has reported a case with similar dilatation of the urinary tract, in which a definite organic obstruction of the nature of a valve in the posterior urethra was found, to account for the back pressure.

The following case report has a threefold purpose; first, to report a case of renal dwarfism; second, to call further attention to the association of this syndrome with an unexplained dilatation of the urinary tract, as described by Ellis and Evans, in contrast to that reported by Ellis, and, third, to direct attention to changes in the pituitary gland with a view to their possible bearing on the development of the dwarfism.

Case Report

D. K., a male, first came under observation at the Hospital for Sick Children in May 1926 at the age of eight years, with symptoms of cystitis and pyelitis of two weeks' duration, and a history of polydypsia and polyuria dating from 12 months of age, excessive in character both day and night. At birth he was normal in size and development. At four years he had measles and at six, whooping cough.

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From the Department of Pathology, University of Toronto.

On examination he was described as poorly developed and emaciated with normal intelligence, an irritable cough and slight naso-pharyngitis. The bladder was distended to the umbilicus. The urine showed 1 + albumin and a specific gravity of 1.002 on three examinations. Pus and *B. coli* were identified. Blood examination showed hemoglobin 65 per cent; red blood cells 3,900,000; white blood cells 34,000. Differential count: 82 per cent polymorphonuclears and 18 per cent lymphocytes. He was discharged one week later much improved.

The next note was that at the age of 13 years and again about one year later at 14, he had attacks of short duration, described as cystitis.

He was finally admitted to the Toronto General Hospital in December 1934, at 16 years of age because of difficulty in breathing of two days' duration. History obtained from relatives at this time stated that for the past two months it had been noticed that he appeared tired all the time and drowsy. This was sufficiently marked to keep him from school, for the first time. He complained of cramps in his legs, numbness of his hands, and after laying down objects held by the fingers, they would stay "flexed" for a short time. For the past month he had had a head cold, a non-productive cough and considerable nasal discharge. Since one year of age he had drunk large quantities of water and passed large quantities of urine throughout the same interval. For the week prior to admission his polydypsia had markedly decreased. The breathing difficulty began two days ago and his physician took swabs and administered 60,000 units of diphtheria antitoxin. The swabs were negative.

It is noted that this boy began school at eight years, was quite bright as a student, never missing an examination. He played with, and acted like, boys of his own age, but he has not grown for the last seven years. The family history was negative.

On examination he was described as a small red haired boy appearing of about half the stated age, conscious, very hoarse, breathing with considerable difficulty. The respirations were rapid and stertorous, with prolonged expiration. Râles were heard in both lungs. Examinations of the heart and of the abdomen were essentially negative. The external genitalia were undeveloped, with no pubic hair, and the testicles undescended. The nervous system was negative. No urine could be obtained. The blood showed a hemoglobin of 70 per cent; red blood cells 4,200,000; white blood cells 24,000. Non-protein nitrogen, 111 mg. per cent; CO_2 combining power 10 per cent; fasting blood sugar 0.07 per cent; serum S.N.P., 2 +. The Wassermann was not taken. The patient died in a generalized convulsion shortly after admission to hospital, before further examination could be carried out.

Summary of Postmortem Findings. Symmetrical, dwarfed male of juvenile appearance without secondary sex characteristics. Measured 134 cm. in length and was estimated to weigh 85 lbs. Trunk, head and limbs well proportioned and symmetrical. Skin soft, smooth and elastic with moderate amount of subcutaneous fat. Teeth in good condition. No skeletal deformity. Testicles undescended, no pubic hair. Redundant prepuce. Brain weighed 1450 grams, slight edema, vessels normal. The pituitary gland only half filled the sella turcica. It was small, rounded, weighed 0.20 gram and showed no evidence of tumor. The anterior and posterior lobes were of normal proportions to each other. The accessory nasal sinuses were free of infection. The mucosa of the trachea, larynx and epiglottis was reddened, edematous, irregularly eroded and covered with a pseudomembranous deposit. The thyroid was small, weighing only 10 grams but was normal in appearance. The thymus was of normal appearance and weighed 14 grams. The lungs showed an early bronchopneumonia at both bases. The heart appeared normal, showing no hypertrophy. The aorta, radials and femoral arteries showed no abnormality. There was a slight amount of clear fluid in the peritoneal cavity. Spleen, liver and gastrointestinal tract were normal. Adrenals large, weighing 8.75 grams each, but of normal appearance. The testes were in the inguinal canals, small, soft, each the size of a lima bean, weighing together 4.5 grams.

Genito-Urinary Tract. The kidneys were slightly larger than usual, flabby and embedded in a considerable amount of fat. The right measured 11 by 6 by 2.8 cm., and the left 10.2 by 5 by 2.8 cm. The capsules were adherent, the surfaces, nodular and cystic. On the cut surface the kidney tissue, largely replaced by large, cyst-like dilatations of the calyces containing a cloudy fluid, appeared as a tough white shell. The cortex and medulla could not be differentiated. There were no abscesses or streaky suppuration as seen in acute pyelonephritis. The pelves were large dilated sacs, and both ureters were widely dilated, measuring up to 3.5 cm. in circumference. There was no obstruction in the ureters and each could be readily traced into the bladder. The bladder wall was greatly hypertrophied, trabeculated. The mucosa was pale, smooth with occasional areas of congestion.

No obstruction was found in the prostatic urethra, although the urethra was transected after examination from the bladder end. The penis was removed and the urethra opened carefully but no point of obstruction could be found.

Microscopically the kidney showed great reduction in the number of glomeruli, those in the outer cortical zone being completely fibrosed, while in the deeper portions, those remaining showed marked variation in size with pronounced thickening of the capsular membrane. There was marked separation and extensive loss of tubules due to a great increase of fibrous tissue. Some of the remaining tubules contained hyaline casts. In several areas there were focal collections of lymphocytes and polymorphonuclear leukocytes, and in addition lymphocytes were scattered diffusely throughout the interstitial tissue. The blood vessels were not markedly thickened.

The pituitary gland showed a symmetrical atrophy, the relative proportions of anterior to posterior lobe being essentially the same as in the normal hypophysis. In the anterior lobe, the acidophilic cells were abundant but not evenly distributed, there being a definite tendency to clumping without any specific relation to blood sinuses. The chromophobes were increased in number, being equal to, if not greater than, the number of acidophile cells. There were relatively few basophiles distributed about the peripheral portions of the lobe, but they were more abundant in the region of the stalk.

Search of the thyroid and adjacent tissues revealed one large parathyroid gland measuring 4 by 2 mm. Microscopically the cells were all of one type, the large clear chief cells. No acidophilic (oxyphil) cells were seen. A few scattered collections of fat cells were present.

The testis showed a definite increase in the number of interstitial cells. The seminiferous tubules, however, were juvenile in type, the lining cells being limited, for the most part, to a single layer of epithelial cells, the spermatogoönia and sertoli cells. In some instances spermatocytes of the secondary layer could be made out, but no further stage of spermatogenesis was evident.

A section of the spinal column at the level of the first lumbar vertebra showed between the cartilaginous plate and the cancellous bone an irregular line of endochondral osteogenesis. The normal arrangement of the cartilage cells in columns was partially destroyed. The bony trabeculae were irregular and thicker than normal, showing water marking to quite a marked degree, each containing a central core of irregular moth-eaten bluish staining matrix and an outer smooth layer involved in patchy areas by small buds of cellular connective tissue containing osteoclasts. The marrow appeared normal.

Microscopically all the other organs were without any significant pathological change.

Discussion

Of the many interesting pathological features of this case, one of the most striking was the occurrence of an unexplained dilatation of the urinary tract.

Undoubtedly some obstructing factor or mechanism was present, and its apparent site was obviously at the bladder neck or below this level, as the bladder was uniformly hypertrophied. Unfortunately, in our case the entire urinary tract, including the urethra, was not removed in continuity, the urethra being severed just below the prostate. Consequently, though careful examination of the prostatic urethra, and subsequently the penile urethra, failed to establish any cause for the obstruction, the possibility, as pointed out by Poynton and Sheldon,[6] that the method of removal destroyed the evidence, such as a valve or incomplete septum at the site of transection, is naturally to be considered. These authors believe that most of these cases are the result of definite organic obstruction rather than a functional disorder of the neuro-muscular mechanism controlling the urethro-vesical sphincter, as suggested by Ellis and Evans.

That clinical evidence of such an obstruction in the posterior urethra may be entirely lacking, was shown by Hinman and Kutzman [7] who collected 50 reported cases of congenital valvular obstruction of the posterior urethra. They found that frequently the characteristic symptoms such as dribbling, incontinence, and dysuria did not become obvious until infection of the dilated urinary tract occurred. This was borne out by the case of Ellis, but in our case, though infection was undoubtedly present, at no time were symptoms of obstruction present, even as a terminal event.

The suggestion that infection may be the primary factor was mentioned by Mitchell [8] as a possible explanation of these cases of dilatation without any organic lesion. Obviously this is in contrast to the usual sequence of events, and the origin of the infection remains therefore to be explained.

The many other cited causes which might lead to obstruction, such as congenital torsion of the penis, phimosis, atresia of the urethra, congenital hypertrophy of the vera montanum, cysts of the urethral mucosa and prostate, were not operative in this case. Mitchell quotes Sawyer as having had two cases in which he attributed the obstruction to a long prepuce. In our case there was a redundant prepuce, but such a cause is untenable, in view of the fact that many such conditions are present in infancy and unless complicated by some other factor, such as phimosis, do not lead to obstruction.

The kidney findings in this case suggest the changes of both chronic interstitial nephritis and ascending infection. It is obviously difficult, however, to determine what part in the production of these lesions was played by each of these two conditions; nor is it possible to say which was the primary factor.

Due to the insidious onset and long protracted course of the disease, these children do not, as a rule, come under observation until either lack of development or bone deformities become evident. The early history of thirst and polyuria provides interesting data for speculation. There is some evidence according to Mitchell that congenital nephritis may occur, and Ellis suggests that both the dilatation and nephritis may have that origin. He further points out that if the chronic nephritis is a result of back pressure in previously normal kidneys, the type of obstruction which would produce such a result would appear to be one of slight degree.

The solution of the entire problem lies in a much earlier and closer examination of these children before the advanced changes in the urinary tract so obscure the picture that the true etiological basis cannot be determined.

The dwarfism occurring in these cases has been almost universally attributed to an altered metabolism as a result of the long standing renal insufficiency. Its mode of production has never been explained. Throughout the literature, little or no reference has been made to the pituitary gland, beyond the statement that in some instances it was either normal or smaller than normal. The first clear suggestion came from Hutinel [9] who described a typical case of renal rickets which at postmortem did not show any interstitial nephritis, and he regarded the dystrophy as due to an alteration of the glands of internal secretion, particularly the hypophysis.

In Ellis and Evans' series, the pituitary was mentioned only in case 7, in which a cyst was found on the superficial aspect of the pars intermedia. R. W. B. Ellis stated in his case that the appearance of the pituitary was within normal limits. A roentgenogram on the skull of a case reported by Zundell [10] showed a normal pituitary fossa. Feiling and Holyoak [11] noted that in their case, though no definite abnormality could be seen, the sella turcica was small and ill-developed.

In those cases of dwarfism where the pituitary is primarily at fault, the anterior lobe deficiency is inherited and in most cases there is a definite family history. Moreover the cases are recognized early. On the other hand, the dwarfism occurring in these renal cases is not apparent for some time. Usually they are normal at birth and continue so until about the seventh year after which time the retardation in growth slowly becomes evident.

In the light of our present knowledge, interpretation of the findings in the pituitary, though suggestive, are inadequate and naturally open to much criticism. They are, however, extremely interesting, and for that reason merit consideration.

If, as Bell [12] points out, the cellular constituents of the anterior lobe represent different stages in the activity of a single cell type, namely, the acidophilic cells indicating the secretory phase, the basophilic a storage phase, and the chromophobes the resting or exhaustion phase, the predominance here of the chromophobic cells might be interpreted as indicative of an exhaustion phase in the gland. What, if any, significance can be attached to the peculiar clumping of the acidophilic cells is impossible at present to say. Their numbers showed no definite increase or decrease.

Rasmussen [13] has shown in numerical counts on normal glands that the chromophobes may constitute as high as 57 per cent of the anterior lobe cells, with an average of approximately 52 per cent, and a comparatively wide range of variation. Also that the chromophile series may show considerable variation, though not to so marked a degree. In view of these normal variations any approach from the numerical angle, in disease states, must be made with caution before assigning to the results any pathological significance.

These observations were made, however, on normal adult glands, and it does not follow that equivalent conditions obtain in the actively growing period of the first decade.

The suggestion is made that this exhausted and atrophied gland may be the result of a secondary effect exerted upon it by some single or complex product arising as a result of the slowly increasing metabolic disturbance, consequent on the renal disease. A point is reached when there is a relative anterior lobe insufficiency, that is, the demand exceeds the supply, and consequently there is a slow but progressive retardation of somatic, genital and osseous growth.

The bone changes in these cases are interesting, particularly as regards their frequency, mode of origin, and the question whether they are identical with those described in true infantile rickets.

The high incidence and sudden onset of the bone deformities have been well described by Barber,[14] Parsons,[15] Lathrop,[16] and Mitchell. The average age at which they develop would seem to be about the ninth year, and their importance is reflected in the fact that their presence may be the first evidence of the true underlying condition. Of these deformities, genu valgum is the most frequent and most important. Barber further points out that the deformities are uncommon in the first few years of life, and in many instances have only appeared at puberty. In the case described by Ellis the typical deformity occurred relatively early, at four years and 10 months, while in our case there was no clinical evidence of any bone deformity, and it was not until examination of a section taken from the vertebral column at postmortem, that definite bone changes were found. Unfortunately, important clinical data such as serum calcium and phosphorus estimations and radiological studies of the long bones were not obtained, attention being particularly directed toward the treatment of the acute uremic state.

Most of the discussion and speculation directed toward an understanding of the fundamental problems in the so-called cases of renal rickets have to do with the chemical changes in the blood, with particular emphasis laid on the relative concentrations of the inorganic phosphorus and calcium.

The usual finding has been a raised serum phosphorus due to the extreme functional disability of the kidney to excrete phosphate, and a lowered serum calcium consequent on the hyperphosphatemia (Peters and Van Slyke[17]). Based on this altered ratio, Lathrop, and Shepley, Park, McCollum and Simmonds[18] have suggested that renal dwarfism is a type of low calcium rickets which results from the effects of high serum phosphorus on serum calcium and calcification. The studies of Boyd, Courtney and MacLachlan,[19] Schoenthal[20] and Parsons support this view. On the other hand, Hunter[21] states that "The theory that phosphate retention, due to the renal defect is primarily responsible for the changes in the bones is clearly unsatisfactory." He further points out that in rickets there is a disturbance of exogenous metabolism resulting in a deficient calcification of osteoid tissue, because of a lack of proper metabolism of calcium and phosphorus in the absence of vitamin D; whereas, in renal rickets, though the bone changes may be identical with true rickets, here vitamin D is not lacking and the changes in bones are due to a disturbance of endogenous metabolism of calcium and phosphorus, for which the renal insufficiency, as a result of the chronic nephritis or its equivalent chronic renal obstruction, is responsible.

Two very interesting studies dealing with parathyroid involvement in these cases were made by Smyth and Goldman[22] and Langmead and Orr.[23] The former authors, reporting a case of renal rickets, parathyroid dysfunction and metastatic calcification in a boy of 14 years, the underlying cause of which was a congenital urethral obstruction, found that the retention of acid phosphate constituted the first important change in the blood chemistry and, while agreeing with the theory based on the high level of blood phosphorus, suggest that the raised serum phosphorus stimulates the parathyroid glands (parathyroid hyperplasia) resulting in dwarfism and demineralization of the bones. Langmead

and Orr suggest as an explanation of the bone changes that although the chronic renal disease occurring in renal dwarfism may cause true rachitic changes in bones, the most characteristic osseous changes seen radiographically are due to osteoclastic resorption, the result of secondary parathyroid activity.

Mitchell, from his extensive review of the literature concluded that clinically the bone changes were identical with those seen in the usual infantile rickets but that radiologically and histologically they appear somewhat different. With regard to the latter, Brockman's study of the histological changes would seem to indicate that although both show the irregular line of ossification with formation of irregular bony trabeculae, destruction of cartilage cells, increased number of blood capillaries, and replacement of red marrow in relation to the trabeculae, with fibrous tissue, in renal rickets these changes are much more marked, with slight differences sufficiently evident to distinguish between them.

In our case we feel, therefore, that the changes described do not warrant any definite conclusion as to the possibility of their being rachitic in type, but that they merely indicate a general inhibition of growth.

Summary

1. A case of renal dwarfism is reported.

2. The interesting finding of a marked dilatation of the urinary tract and hypertrophy of the bladder, unsuspected clinically, is discussed.

3. The urinary retention appeared to occur at the level of the urethro-vesical sphincter. No obvious organic cause for the obstruction was found.

4. Of particular interest were the marked changes in the pituitary gland, and the hypothesis is suggested that the dwarfism may be due to a secondary effect on the pituitary of some product of altered metabolism arising as a result of the long standing renal insufficiency.

5. Definite microscopic changes in the bone of the vertebral column are described and are interpreted as evidence of a general inhibition of growth.

REFERENCES

1. Fletcher, H. M.: Case of infantilism with polyuria and chronic renal disease, Proc. Roy. Soc. Med. (Sect. Dis. Child.), 1911, iv, 95.
2. Lucas, C.: A form of late rickets associated with albuminuria, Lancet, 1883, i, 993.
3. Barber, H.: Renal dwarfism, Quart. Jr. Med., 1920, xiv, 205.
4. Ellis, A., and Evans, H.: Renal dwarfism, Quart. Jr. Med., 1933, 231.
5. Ellis, R. W. B.: Renal dwarfism, Lancet, 1935, i, 142.
6. Poynton, F. J., and Sheldon, W. P. H.: On dilatation of the bladder and ureters in childhood, Arch. Dis. Child., 1927, ii, 251.
7. Hinman, F., and Kutzman, A. A.: Congenital valvular obstruction of the posterior urethra, Jr. Urol., 1925, xiv, 71.
8. Mitchell, A. G.: Nephrosclerosis (chronic interstitial nephritis) in childhood, Am. Jr. Dis. Child., 1930, xl, 101, 343.
9. Hutinel, V.: *Abstr.* in Brit. Jr. Child. Dis., 1912, ix, 513.
10. Zundell, C. E.: Two cases of infantilism, Proc. Roy. Soc. Med. (Sect. Dis. Child.), 1913, vii, 1.
11. Feiling, A., and Holyoak, W. L.: Case of renal dwarfism with optic atrophy, Proc. Roy. Soc. Med. (Clin. Sect.), 1921, xv, 1.
12. Bell, B.: The pituitary, 1919, Baillière, Tindall and Cox, London.

13. Rasmussen, A. T.: The percentage of the different types of cells in the male adult human hypophysis, Am. Jr. Path., 1929, v, 263.
14. Barber, H.: The bone deformities of renal dwarfism, Lancet, 1920, i, 18. Renal dwarfism, Guy's Hosp. Rep., 1922, lxxii, 62. Renal dwarfism, Guy's Hosp. Rep., 1926, lxxvi, 307.
15. Parsons, L. G.: The bone changes occurring in renal and coeliac infantilism, and their relationship to rickets, Arch. Dis. Child., 1927, ii, 1, 198.
16. Lathrop, F. W.: Renal dwarfism, Arch. Int. Med., 1926, xxxviii, 612.
17. Peters, J. P., and Van Slyke, D. D.: Quantitative clinical chemistry, 1931, Williams and Wilkins Co., Baltimore.
18. Shepley, P. G., Park, E. A., McCollum, E. V., and Simmonds, N.: Is there more than one kind of rickets? Am. Jr. Dis. Child., 1922, xxiii, 91.
19. Boyd, G. L., Courtney, A. M., and MacLachlan, I. F.: The metabolism of salts in nephritis, Am. Jr. Dis. Child., 1926, xxxii, 29.
20. Schoenthal, L., and Burpee, C.: Renal rickets, Am. Jr. Dis. Child., 1930, xxxix, 517.
21. Hunter, D.: Critical review: the metabolism of calcium and phosphorus and the parathyroids in health and disease, Quart. Jr. Med., 1931, xxiv, 393.
22. Smyth, F. S., and Goldman, L.: Renal rickets with metastatic calcification and parathyroid dysfunction, Am. Jr. Dis. Child., 1934, xlviii, 596.
23. Langmead, F. S., and Orr, J. W.: Renal rickets associated with parathyroid hyperplasia, Arch. Dis. Child., 1933, viii, 265.

ACUTE FULMINATING MENINGOCOCCUS INFECTION WITH BILATERAL CAPILLARY HEMORRHAGE OF THE ADRENALS AS THE MOST STRIKING GROSS PATHOLOGIC LESION; A CASE REPORT*

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The case I shall report died 12 hours after the onset of the final illness, one-half hour after admission to the Walter Reed General Hospital. The antemortem diagnosis was Rocky Mountain spotted fever. As no antemortem laboratory work of any kind had been done and as only a very superficial physical examination had been possible, the microscopical studies on the autopsy material were undertaken to substantiate or refute the original diagnosis. The final diagnosis was not made until after a careful microscopical examination of the body tissues had been completed. The author deems the case especially valuable as an illustration of the solution of a problem in postmortem diagnosis.

Case Report

W. H., a white male, aged 20 years. A member of the Civilian Conservation Corps, attached to Camp A2, Beltsville, Md. He always had been in good health and exceptionally strong and active. He worked Saturday, Sept. 21, 1935, until noon when he was given a pass for the weekend. According to the statement of the patient's brother the patient was perfectly well until Sunday evening. Sunday evening, September 22, the patient "suddenly came down with chills and fever, and brown spots appeared over his body; he complained of pain in his joints." The family physician was called who made the diagnosis of Rocky Mountain spotted

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From the Laboratory Service, Walter Reed General Hospital, Washington, D. C.

fever. Monday morning, September 23, the patient's brother transported him in an automobile from Landsdowne, Md., to Camp A2, arriving at the Camp Dispensary at 8:30 a.m. At this time the patient presented the picture of a hemorrhagic purpura involving practically the entire body. He was conscious, answered questions intelligently and did not appear to be in great pain. He was immediately transferred to the Walter Reed General Hospital, Washington, D. C.

The patient was admitted to the Walter Reed General Hospital, Monday, September 23, at 9:45 a.m. He presented what was described by the Ward Surgeon as a hemorrhagic discoloration of the skin over the entire body. Conjunctivae hemorrhagic. Pupils equal in mid-dilatation. Lips cyanosed. Pulse almost imperceptible. The heart sounds were distant and the blood pressure too low to determine. The patient became comatose within 15 minutes after admission. He vomited about 250 c.c. of "greenish mucus." He died at 10:15 a.m., one-half hour after admission to hospital.

Autopsy, W. R. G. H. Autopsied September 23, 1935 at 10:45 a.m., 30 minutes after death. The following is an abstract of the protocol:

Body that of young adult white male, length 174 cm., weight 77 kg. Well nourished; voluntary musculature exceptionally well developed. Right pupil 6 mm. in diameter; left 5 mm. No exophthalmos. There is marked subconjunctival hemorrhage, bilateral. The left deltoid region presents two large vaccination scars. The cutaneous surface of the body shows a diffuse erythema, ham colored, most advanced over face, neck, arms and extensor surfaces of forearms. Ears cyanosed. The thighs and legs are only slightly "flushed." The palmar surfaces of the hands and feet are of normal hue. After removal of the viscera and consequent drainage of blood, the cutaneous erythema paled considerably leaving scattered bluish petechial areas over the forehead and surrounding the mouth.

Thymus rest: 25 gm. Thyroid: 25 gm. Congested.

Lungs: Right 450, left 400 gm. Upon the pleural surface of all lobes both lungs are scattered small bright red points of hemorrhage, 1 to 2 mm. in diameter. *Heart:* 370 gm. The epicardial surface presents scattered points of hemorrhage. The wall of the left ventricle is 1.9 to 1.4 cm. in thickness; cut surfaces grayish-red; consistence firm. The aortic ring is 6.5 cm. in circumference. The valves are normal. The heart contains fluid blood. The coronaries are normal. Aorta: intima smooth, glistening and of a normal ivory hue.

Abdomen: There are widely scattered, small points of hemorrhage over the stomach, jejunum and ileum and over both leaves of the mesentery of the small gut. There is no increase in fluid in the peritoneal chink. Stomach: Slightly dilated. Mucosa grayish-red, rugae preserved. No eschars, no ulcers. The lumen of the stomach contains 250 c.c. of grass green fluid without appreciable odor. Jejunum: Wall slightly edematous; mucosa pink, glistening and shows normal markings. The mucosa presents a few petechial hemorrhages, 2 to 4 mm. in diameter. The lumen contains a small amount of semi-solid pale yellow material. Ileum: Contracted, contents scant in amount and of pale yellow hue. The mucosa of the lower ileum presents six to eight oval areas measuring from 1 to 3 cm. in length, long axes paralleling the long axis of the bowel. The oval areas are grayish, finely granular and lusterless; edges sharp. Vermiform appendix: Normal in the gross. Colon: The ascending, transverse and descending colon are contracted; mucosa pale, moist and glistening. There are a few scattered petechial hemorrhages, 2 to 4 mm. in diameter, bright red in color, located in the mucosa. The rectum and sigmoid contain fluid feces; no gross blood. The mucosa lining the rectum is pale gray and presents scattered petechiae and innumerable pin-point hemorrhages. The lymph nodes in the mesentery of the small gut are enlarged to the size of split peas; pinkish-gray and shotty to the feel. Liver: 1630 gm. No gross pathology. Spleen: 160 gm. Consistence firm. Cut sur-

faces flat, glistening and of a deep plum color. Corpuscles not visible in the gross. Pancreas: 110 gm. Normal in the gross.

Adrenals: The adrenals furnish a striking gross appearance. The combined weight of the two adrenals is 25 gm. (normal 12 to 15 gm.). They are of normal contour, firm and of a dark slate color. The cut surfaces show marked capillary hemorrhage throughout the cortices and invading the medullary portions. The cut surfaces of the adrenals are flat and of a reddish brown hue. Small islands of grayish translucent medullary parenchyma are visible. Both adrenals present the same gross picture. (Figures 1 and 2.)

Kidneys: Right 170, left 180 gm. Cut surfaces show moderate congestion. Urinary bladder, prostate, seminal vesicles, vasa deferentia and testes: Normal in the gross.

Calvarium: Normal. Dura: Moderate edema. Brain: 1370 gm. Consistence quite soft. The pia is congested. The ependyma is smooth and glistening. There is marked congestion of the small vessels beneath the ependyma covering the floor of the fourth ventricle. Pituitary: Normal. The circle of Willis and cerebral arteries present normal walls and contain fluid blood.

The outstanding gross findings are: (1) cutaneous erythema with purpuric areas; (2) scattered points of capillary hemorrhage upon the serous surfaces of the viscera; (3) hyperplastic Peyer's patches and enlarged mesenteric lymph nodes; (4) bilateral capillary adrenal hemorrhage; (5) congestion of the pia arachnoid.

Considering the above gross findings singly the diagnoses suggested are: Rocky Mountain spotted fever; typhoid fever; bilateral capillary hemorrhage of the adrenal, possibly toxic as in diphtheria, possibly septic; bulbar palsy. The final diagnosis was not made until the above possibilities were eliminated.

As suggested by the gross pathological findings, the following bacteriological examinations were made:

(a) Cultures from the nares and the nasopharynx upon Loeffler's medium were negative for the diphtheria bacillus.

(b) Culture from the heart's blood was overgrown by *B. coli.*

(c) Culture from spleen showed no growth.

(d) Cultures from the contents of the lower ileum, caput coli and from the surfaces of the Peyer's patches all were negative for bacilli of the typhoid-dysentery groups.

Blood serum of the deceased was agglutinated against *B. proteus* X-2, proteus X-19 and proteus Kingsbury; all agglutinations were negative.

Blood taken from a subcutaneous venule of the cadaver shows the following differential count: lymphocytes 38, monocytes 17, neutrophiles 45 per cent. The lymphocytes are all of the small type. The neutrophiles are 28 per cent band forms and 17 per cent segmented forms. The granulocytes present advanced degenerative changes. Gram stain of blood film shows no microörganisms.

Microscopical examinations were made of all the organs of the body, stained both by H. E. and Giemsa. Especial attention was paid to the reaction of the blood vessels of the skin, brain and heart in view of the original diagnosis of Rocky Mountain spotted fever.[1, 2] There is no endothelial swelling or hyperplasia and no thrombosis. The perivascular reaction is limited to the skin where there is engorgement of the venules in the zone between the corium and hypodermis; the congested subpapillary venules present an irregular piling up of the adventitial cells including a considerable number of mast cells and an occasional lymphocyte. The capillaries supplying the sweat glands and the papillae of the hair follicles show no pathologic changes. None of the histiocytes or endothelial cells include Rickettsia. There are no perivascular nodules in the heart, and sections of the testes show normal histology. The histopathology of Rocky Mountain spotted fever was fresh in my mind due to a case autopsied recently. Dr. R. D. Lillie of the National Institute of Health kindly studied

FIG. 1. *Adrenals:* combined weight 25 gm. Dark slate color in the gross.

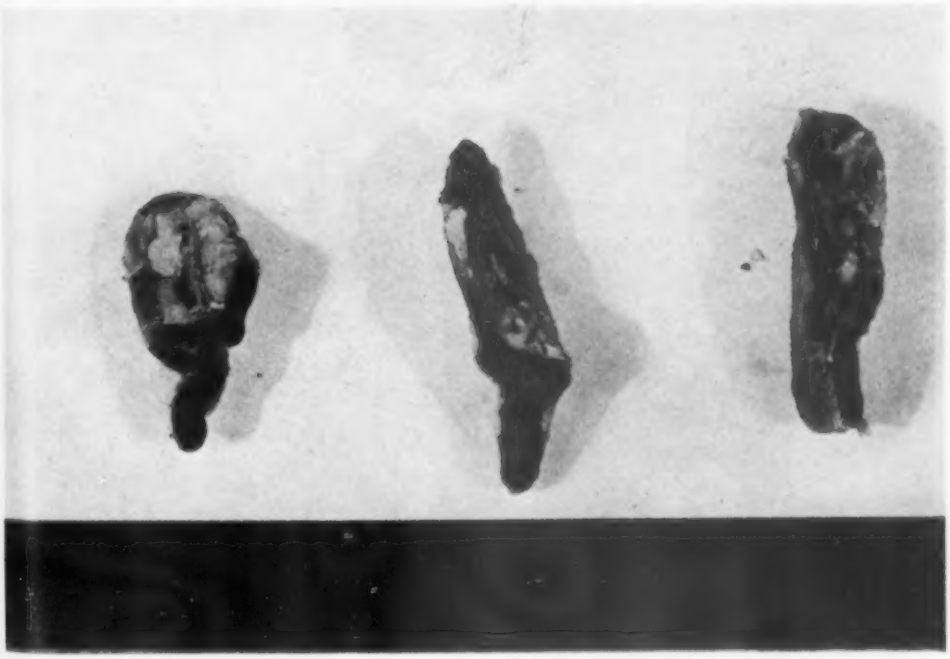

FIG. 2. *Adrenal:* cut surfaces flat, reddish-brown, markings greatly obscured.

the slides I made in the case I am now reporting and found nothing suggestive of Rocky Mountain spotted fever.

The micro-sections of the lower ileum show hyperplasia of the Peyer's patches; the germinal centers are prominent and present small areas of karyorrhexis and beginning necrosis (figure 3). No bacteria are revealed by the Giemsa stain. The

FIG. 3. *Lower ileum* × 105. H. E. Stain. Shows the marked hyperplasia of the Peyer's patches.

lymph nodules in the mesentery of the ileum present large germinal centers; the sinusoids do not show the large swollen phagocytic reticular cells found in the lymph nodes in cases of Rocky Mountain spotted fever.

Adrenals: The surrounding fat presents a diffuse, very slightly marked infiltration with erythrocytes. The arteries show normal walls; the veins are congested. The adrenal capsule is thin and intact. The zona glomerulosa is fairly well represented. Beneath the capsule there is marked capillary hemorrhage extending inward in broad rays and wedge-shaped areas. The remnants of cortex are well preserved; the cells rich in lipoids. The zona reticularis is entirely replaced by hemorrhage. (Figure 4.) The medullary portion is for the most part destroyed by hemorrhage though there are scattered islands of parenchyma remaining. The intact portions of the medulla show capillary congestion, edema, and small agminations of lymphocytes and plasma cells. Sections stained by Giemsa and by Gram reveal no microörganisms. Sections stained by Levaditi show no treponemata.

The microscopic examination of thyroid tissue reveals large acini filled with deeply stained, homogeneous colloid; epithelium flattened. No apical vacuoles. No lymphoid reaction.

The parathyroid section includes a lobule composed of high cylindrical clear cells. The majority of the lobules present alveoli composed of small clear cells; the large polygonal oxyphilic cells are very few in number.

Pituitary: No pathologic changes other than venous capillary congestion.

Brain: Sections were taken from the medulla at the level of the decussation of the pyramids and at the level of the inferior olive and sensory decussation; also from the cortex of the forebrain (left precentral gyrus), the basal ganglion, left, including the internal capsule, caudate nucleus and ependyma lining the lateral ventricle. The sections were stained by H. E. and by Giemsa. The microscopic picture shows congestion of the veins and capillaries in the arachnoid; edema of the molecular layer which includes swollen astrocytes. There is capillary congestion throughout the gray substance and a few small hemorrhages into the perivascular spaces of His. No ring shaped hemorrhages. No thrombosis. No cellular infiltration of the spaces of Virchow-Robin and no perivascular cellular "cuffing."

Sections of the brain stained by Gram show many small Gram-negative diplococci arranged in small groups and in scattered pairs, mostly extracellular though a few of the diplococci are included in the bodies of adventitial cells. The Gram negative diplococci are coffee bean shaped, without capsules and are found in the cellules of the arachnoid over the ventral surface of the medulla and over the outer surface of the forebrain. (Figure 5.)

Gram stain made of the sections of the skin and adrenal reveal no bacteria.

Diagnoses: Acute fulminating meningococcus infection with general purpura and massive bilateral capillary adrenal hemorrhage. *Death* occurred before the onset of a suppurative meningeal reaction.

The bilateral adrenal hemorrhage is very striking, and at one period in the study of the case I was tempted to call the adrenal hemorrhage the cause of death without searching further for a cause of the general pathologic process. The histogenesis [3] of the adrenals and the dual function [4, 5] of these organs should be reviewed by those who are interested in the adrenal lesions encountered in the case I have just presented. The subject of bilateral adrenal hemorrhage had been brought to my attention by Lavenson [6] and by Pearl and Brunn.[7] The adrenal hemorrhage in the cases cited by these authors is of the thrombotic type, secondary to a local inflammatory reaction in the case of Lavenson; possibly syphilitic in the case cited by Pearl and Brunn. The bilateral adrenal hemorrhage in the case I have reported in this paper is of the capillary type, suggesting a toxemia as in diphtheria or a fulminating septicemia. The case of Rocky Mountain spotted fever recently autopsied at this hospital presented unilateral adrenal hemorrhage of the thrombotic type. Whether or not the adrenal damage

FIG. 4. *Adrenal cortex* × 810. H. E. Stain. Shows marked capillary congestion and hemorrhage and destruction of the cortical parenchyma.

in the case I have just reported had any direct bearing upon the rapidly fatal termination, is problematical. Brasser [8] (quoted by Pearl and Brunn) states that massive bilateral adrenal hemorrhage causes an initial hyperadrenalemia followed by hypoadrenalemia resulting in death.

The original diagnosis of the case I have just presented was Rocky Mountain spotted fever, suggested by the cutaneous eruption and no doubt by the fact that cases of this disease had been recently encountered in this section of the United States. In the course of my microscopical examinations I excluded Rocky Mountain spotted fever as the final diagnosis. The negative Weil-Felix reaction here means nothing because of the very short period of time elapsed since

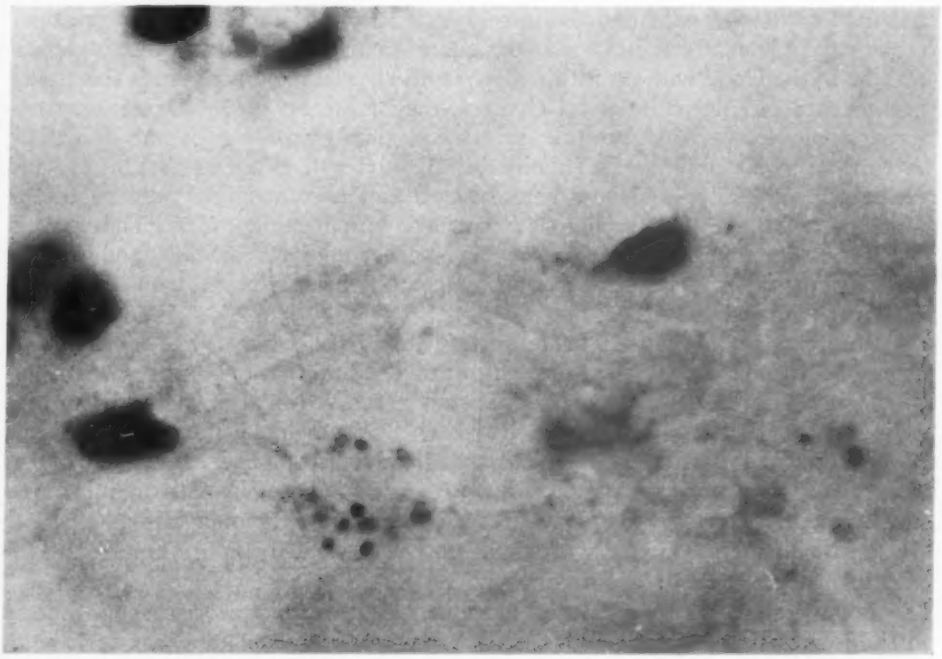

FIG. 5. *Arachnoid*, ventral surface of the medulla oblongata, level of the pyramids × 2050. Gram stain. Shows Gram-negative diplococci in clumps without associated inflammatory reaction other than presence of few lymphocytes and wandering histiocytes.

the onset of the illness. Cecil [9] quotes Wolbach as follows: "In Rocky Mountain spotted fever the rash appears usually on the third to fifth day of the fever. The rash appears first on the wrists, ankles and back; then on the forehead, arms, legs, chest and abdomen. The efflorescence requires 24 to 36 hours. The macules are at first bright red, rapidly become darker and after a few days the eruption is definitely petechial." In the case just presented the eruption came on within a few hours following the initial chill and was general and purpuric from the start.

A typical case of Rocky Mountain spotted fever is presented by Masson.[10] This case will serve well as a model in both the diagnosis and differential diagnosis between Rocky Mountain spotted fever and other exanthemata, giving as it does the incubation period (5 days); the mode of onset; the appearance and

distribution of the eruption and the dates and titers of agglutinations of the patient's blood serum against proteus X–19. In Masson's case of Rocky Mountain spotted fever the eruption first appeared upon the wrists and ankles during the third day of the illness and was of the red macular type; on the fourth day of the illness the "rash" became generalized, involving the face, trunk and extremities including the palms and soles.

As all of us had overlooked meningococcus infection as a possible etiologic factor in the case I have presented, I shall quote several of the accepted texts on the subject of epidemic meningitis.

Osler's [11] definition of cerebrospinal fever is "an infectious disease occurring sporadically and in epidemics; caused by the meningococcus; characterized by inflammation of the cerebrospinal meninges and a clinical course of great irregularity. The affection is also designated as spotted fever. Meningococci may be in the blood without meningitis resulting. In malignant cases there may be no characteristic pathological changes, the brain and cord showing only extreme congestion. The intestine sometimes shows swelling of the follicles." According to Nelson [12]: "In fulminating cases the skin, serous membranes and particularly the adrenals show hemorrhages and microscopically the cutaneous blood vessels have been seen to be crowded with meningococci. The Peyer's patches and the mesenteric lymph glands are commonly swollen and the intestinal mucosa may be hemorrhagic. Petechial hemorrhages may be seen on all serous surfaces."

Referring to the notes I made during May 1919, while I was in charge of Army Laboratory No. 1, Neufchateau, France, I find that many cases of meningitis were hospitalized as respiratory diseases, and the final diagnosis of meningitis was made when the patients had been isolated in the influenza wards of Evacuation and Base Hospitals. French pathologists during the early part of the World War reported cases of meningococcic septicemia without meningeal involvement. During Sept. 1918 a case of bronchopneumonia was admitted to Base Hospital No. 6; the sputum of this case yielded a pure culture of the meningococcus, type IV (Pasteur type B).

Boyd [13] states: "In a case of extremely acute meningococcic septicemia in a child which I studied, the only lesion was an extensive bilateral hemorrhage of the adrenals."

Stevens [14] discusses the fulminating type of cerebrospinal fever which he says is comparable to the malignant forms of other specific infections; not uncommon in some epidemics and occasionally met with sporadically. The patient is suddenly stricken, sometimes without the least warning, and quickly passes into a state of collapse. A severe chill, headache, stupor, soon followed by coma, moderate fever, a feeble pulse and an extreme prostration are the usual symptoms and the usual course. A purpuric eruption is present in some cases. Death is inevitable and may take place within 12 hours. Autopsy reveals hyperemia of the membranes of the brain but no pus.

Dr. A. Magruder MacDonald, the Coroner of Washington, D. C., told me that in the epidemic of cerebrospinal meningitis during the winter and spring of 1934 to 1935, there was a high percentage of fulminating cases with a course of from 12 to 24 hours; autopsies revealed no purulent meningeal reaction in these cases.

A recent report [15] of a case very similar to the one I have just presented has come to my attention. By a happy coincidence the case referred to in this paragraph is from the Navy, while my case was under the Army jurisdiction. The Naval case was admitted to the U. S. S. "Relief" from a battleship, March 9, 1935 and died two and a half hours later. As far as could be determined the patient, a white male, aged 18 years, was sick only five hours prior to his death. The antemortem leukocyte count was 5000 with 71 per cent small lymphocytes. The blood film was loaded with Gram-negative diplococci. The antemortem spinal fluid was entirely negative, cell count three. The antemortem blood culture was positive for the meningococcus (type not specified). The autopsy findings in this case show congestion of the meninges but no purulent exudate; there are petechial hemorrhages in the serosa covering all the viscera. The statement is made that "the adrenals are swollen and appear hemorrhagic."

Summary

The case presented is that of a young adult white male who became ill suddenly during the evening of Sept. 22 this year. The onset of the illness was marked by a chill, followed by pain in various joints. By morning a general purpuric erythema had developed. The radial pulse became imperceptible, coma developed and the patient died 10:15 a.m., Sept. 23. The total illness was of less than 12 hours' duration. Autopsy revealed bilateral adrenal capillary hemorrhage as the most striking gross finding. Micro-sections of the brain stained by Gram showed Gram-negative intra- and extracellular diplococci located in the cellules of the arachnoid. There was no purulent reaction of the meninges. The final diagnosis, based on the microscopic autopsy findings, is acute fulminating meningococcus infection.

Conclusions

It is misleading to over-emphasize the importance of any single gross autopsy finding, such as the cutaneous erythema, the petechial hemorrhages in the serosa of the viscera, the bilateral capillary hemorrhage of the adrenals, the hyperplastic Peyer's patches and the congestion of the brain; all of which were well marked gross autopsy findings in the case I have presented. In any case presenting a skin eruption, the character and distribution of the eruption and the time required for complete efflorescence must be taken into consideration. The importance of considering meningococcus infection as a possible cause of death in an illness of less than 12 hours' duration is emphasized.

BIBLIOGRAPHY

1. Wolbach, S. B.: Etiology and pathology of typhus, Research Commission to Poland, Harvard U. Press, Cambridge, Mass.
2. Lillie, R. D.: Pathology of eastern type of Rocky Mountain spotted fever, U. S. Treasury Dept., Public Health Report, 1931, xlvi, 2840–2859.
3. Maximow, A. A., and Bloom, W.: A text book of histology, 1930, W. B. Saunders Co., Philadelphia, 704–709.
4. Engelbach, W.: Endocrine medicine, 1932, Charles C. Thomas, Baltimore, i, 16–17, 170–172.

5. Rowntree, L. G., Greene, C. H., et al.: Treatment of Addison's disease with cortical hormone of suprarenal gland, Jr. Am. Med. Assoc., 1931, xcvii, 1446–1453.
6. Lavenson, R. S.: Acute insufficiency of the suprarenals, Arch. Int. Med., 1908, ii, 62–73.
7. Pearl, F., and Brunn, H.: Suprarenal apoplexy, bilateral, Surg., Gynec. and Obst., 1928, xlvii, 393–400.
8. Brasser, A.: Beitrag zur Kenntnis der Nebennierenblutung, Klin. Wchnschr., 1924, iii, 738. (Quoted by F. Pearl and H. Brunn.)
9. Cecil, LaFayette: A text book of medicine, by Am. authors, 3rd Ed., 1934, W. B. Saunders Co., Philadelphia, 365.
10. Masson, D. M.: Rocky Mountain spotted fever, report of three cases, Proc. Staff Meet. Mayo Clinic, 1935, i, 658–659.
11. Osler, W.: The principles and practice of medicine, 1931, D. Appleton Co., New York and London, 113–114.
12. Nelson's Loose Leaf Medicine, 1930, Thomas Nelson and Sons, New York and London, ii, 51.
13. Boyd, W.: The pathology of internal diseases, 1931, Lea and Febiger, Philadelphia, 722–723.
14. Stevens, A. A.: The practice of medicine, 2nd Ed., 1926, W. B. Saunders Co., Philadelphia, 90.
15. Boone, J. T., and Hall, W. M.: Meningococcal septicemia with a report showing organisms in the direct blood smear, U. S. Naval Med. Bull., 1935, xxxiii, No. 4.

LIPOIDAL HISTIOCYTOMA (FIBROXANTHOMA); REPORT OF A CASE*

By George M. Lewis, M.D., *New York, N. Y.*, and Wilbert Sachs, M.D., *Jersey City, N. J.*

The origin and nature of the xanthoma cell is in doubt.[1] Because of this, its significance is not fully understood. Many observers have noted the rather widespread occurrence of xanthoma-like cells in dermatoses not usually considered among the true xanthomas. In using the term fibroxanthoma, a combination of a fibroma with a xanthoma is implied. Aschoff and Kammer [2] consider that such a unification exists and classify fibroxanthoma as a type of the true xanthomas. Pinkus and Pick [2] contend that the process is more likely due to the ability of tumors of the connective tissue group to become enriched with lipoids. For this reason, they prefer the term fibroma xanthoma or, better still, fibroma lipoidicum. We doubt that it is a disease *sui generis* because it apparently has no characteristic clinical features.

Case Report

J. S., aged 36, a policeman, was first examined in January 1934, regarding a lesion of six months' duration on the right knee. Four years before, he was struck by a trolley-car and severely injured. Besides several dislocations and internal injuries, he sustained many contusions and abrasions, among which was an abraded area at the site of the present lesion. Healing was delayed and a small infiltrated area remained. Six months before his first visit, he tripped on a subway stair and

* Received for publication August 21, 1935.
From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University.

bruised the same area of skin on his right knee. Following this, a lesion appeared and became progressively larger until it reached its present size (figure 1). Bleeding was at times profuse, so that it was necessary to wear a bandage to prevent his clothes becoming soiled.

Examination disclosed a walnut-sized, dark-red nodule, elevated above the surface of the skin. Its surface was uneven and in one part was covered with a crust. There was very slight infiltration at the base. Palpation of the lesion revealed a slightly harder consistency than one would expect from its appearance.

From the clinical characteristics, the lesion was considered either sarcoma or pyogenic granuloma. Because of the possibility of malignancy, it was felt advisable

FIG. 1. Photograph showing the lesion on the right knee.

to excise the lesion. This allowed a complete histologic study to be made. After surgical removal, the wound was closed with three interrupted sutures.

Pathology. In the center of the specimen was an infiltrate occupying one-half the section and extending throughout the upper, mid, and deep cutis down to the fat (figure 2). This infiltrate was composed of closely packed cellular elements. The area was circumscribed and sharply differentiated from the normal tissue on either side.

Throughout the infiltrate were coarse and fine strands of connective tissue. Within these were many blood and lymphatic vessels. In the mid and upper cutis these vessels were more numerous and were markedly dilated; some were filled with blood elements.

At the margins of the section, the epidermis was markedly and irregularly acanthotic. The rete pegs encircled the cellular infiltrate and extended down almost

FIG. 2. Low power photomicrograph showing the lesion as a whole (×10).

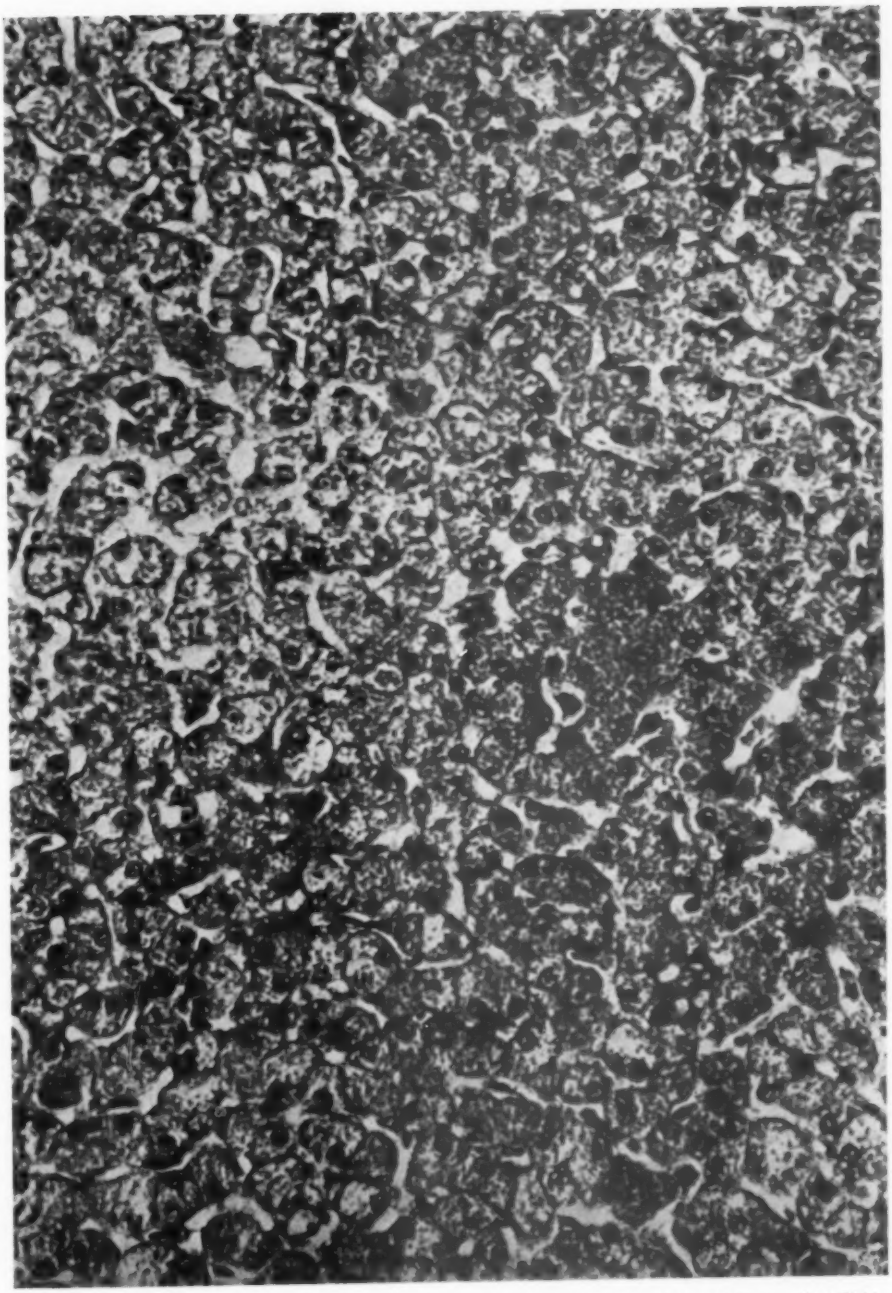

FIG. 3. High power photomicrograph showing histiocytes with fatty changes (× 500).

to the deep cutis. Overlying the cellular mass, the epidermis was thinned into a narrow band of three or four layers of cells, composed of one basal cell, one or two prickle cells, and one horn cell. The rete pegs and papillary bodies were absent. Over the center, the epidermis was entirely missing and the cellular mass extended to the surface.

The infiltrate was composed of large cells, some being round and some polygonal; they were about in equal proportion (figure 3). The cell outlines were distinct and the nuclei were large and round, with chromatic fibers loosely arranged. There were definite nucleoli. Many of the cells contained two or three nuclei. The spongioplasm was fairly clear but the hyaloplasm was only faintly visible, giving a foamy appearance to the cell body.

Besides the presence of xanthoma-like cells, granuloma pyogenicum was differentiated from fibroxanthoma by the absence of granulation tissue and the presence of a different stroma; sarcoma was ruled out by the absence of variously-sized connective tissue cells, by the fact of the lesion being well circumscribed and demarcated and by its orderly arrangement.

Summary

A case is reported in which the clinical findings were suggestive of either granuloma pyogenicum or of sarcoma. The histology was that of fibroxanthoma. Examination of the patient one year following the removal of the lesion revealed no evidence of local recurrence.

BIBLIOGRAPHY

1. Plews, L. W.: The nature and origin of the xanthoma cell, Arch. Path., 1934, xvii, 177. Gruenfeld, G., and Seelig, M. G.: The nature of so-called xanthoma, Arch. Path., 1934, xvii, 546.
2. Urbach, E.: Lipoid metabolism diseases of the skin, Handbuch der Haut und Geschlechtskrankheiten, 1932.

EDITORIALS

THE AMERICAN BOARD OF INTERNAL MEDICINE

During the recent session of the American Medical Association at Kansas City, Missouri, May 11 to 15, 1936, the American Board of Internal Medicine was given final official approval by the Advisory Board for Medical Specialties, the Council on Medical Education and Hospitals and the Section on Practice of Medicine of the American Medical Association.

The Section on Practice of Medicine, American Medical Association, held a special executive meeting for this purpose, preceding the scientific program, Wednesday morning, May 12, 1936 with Dr. William J. Kerr, chairman of the section, presiding. Present on the platform were the four representatives from the Section on the Joint Committee of Organization, Reginald Fitz, Ernest E. Irons, John H. Musser, and Walter L. Bierring as well as Dr. James Alexander Miller, recent president of the American College of Physicians.

The plan of organization of the Board with an outline of the methods for certifying specialists in internal medicine was presented by the chairman of the Joint Committee, Walter L. Bierring; after which Dr. James Alexander Miller made a statement on behalf of the American College of Physicians that the College appreciated the privilege and opportunity to sponsor this movement and coöperate with the Section in the organization of the American Board of Internal Medicine.

The resolution of approval by the Section on Practice of Medicine, American Medical Association, was presented by Dr. James A. Paullin and supported by Dr. S. Marx White, after which it was unanimously adopted.

The historic significance of this action was manifest to all who were present. Within one year after the Regents of the American College of Physicians at the Philadelphia session in 1935 adopted the resolution to underwrite the necessary expense and join with the Section on Practice of the American Medical Association in the organization of a qualifying board for the certification of internists in the United States and Canada, the purpose was accomplished.

The American Board of Internal Medicine comprises nine members with five representatives from the American College of Physicians: Jonathan C. Meakins, O. H. Perry Pepper, David P. Barr, William S. Middleton and G. Gill Richards, and four members representing the Section on Practice of Medicine, American Medical Association, Reginald Fitz, Ernest E. Irons, John H. Musser and Walter L. Bierring.

The first meeting of the Board will be held in Chicago, during the month of June, at which time officers and personnel of special committees will be selected, and plans of procedure regarding methods of qualification and certification adopted. All the activities of the Board will be given the fullest publication in the Annals of Internal Medicine.

THE IMPORTANCE OF POTASSIUM IN THE TREATMENT OF ADDISON'S DISEASE

THE work of Harrop * and of Allers † and others has shown that the adrenalectomized dog may be kept alive indefinitely without the use of cortical hormone by the administration of sufficient quantities of sodium in the forms of sodium chloride and of either sodium bicarbonate or sodium citrate. Recent work of Allers has indicated that if the potassium intake be kept to a very low level, these animals, maintained on a high sodium intake, will not only live but will show entirely normal plasma electrolyte levels.

Adrenalectomized animals maintained on this high sodium, low potassium régime have shown themselves very much more sensitive to the action of a variety of toxic substances than are normal animals. They have been found to be highly sensitive to the action of insulin, of histamine, and of thyroxin. Important observations have now been published which indicate that they are also highly sensitive to the effect of any increase in the potassium intake.

This sensitivity of the adrenalectomized animal to potassium is especially significant since the effect produced is very similar to the acute crisis seen in the untreated animal following adrenalectomy. The prostration of the animal is accompanied by a fall of serum sodium levels and a rise in serum potassium. The color, viscosity, sedimentation rate and clotting time of the blood resemble similar determinations made on the blood in acute crisis following adrenalectomy. Intravenous injections of large amounts of sodium chloride, sodium bicarbonate and glucose plus large amounts of cortin serve to restore these animals to normal.

The importance of these similarities between the crises produced by increasing the potassium intake and those occurring spontaneously is enhanced by the consideration of data indicating that in Addison's disease in periods of crisis the serum potassium rises as the serum sodium falls. The administration of large doses of cortin tends to reverse these phenomena. It would appear, therefore, that the level of potassium in the serum is as intimately concerned with the mechanism of crisis and as much under the regulation of the cortical hormone as is the level of serum sodium.

The practical application of this principle to the control of Addison's disease has been under investigation in the Mayo Clinic and the results obtained in three patients have been published.‡ It was found that when the intake of potassium was kept at 1.6 gm. per day the sodium and chloride intake could be reduced from such figures as 8.1 gm. sodium and 10.9 gm.

* HARROP, G. A., SOFFER, L. J., NICHOLSON, W. M., and STRAUSS, M. B.: Studies on the suprarenal cortex. IV. The effect of sodium salts in sustaining the suprarenalectomized dog, Jr. Exper. Med., 1935, lxi, 839–860.

† ALLERS, W. D.: The influence of diet and mineral metabolism on dogs after suprarenalectomy, Proc. Staff Meet. Mayo Clinic, 1935, x, 406–408.

‡ WILDER, R. M., SNELL, A. M., KEPLER, E. J., RYNEARSON, E. H., ADAMS, M., and KENDALL, E. C.: Control of Addison's disease with a diet restricted in potassium: a clinical study, Proc. Staff Meet. Mayo Clinic, 1936, xi, 273–283.

chloride to 6 gm. of sodium chloride daily without seriously altering the levels of serum sodium or serum potassium and without producing clinical evidence of crisis.

On the other hand when the patients were in normal condition on a régime of high sodium and chloride and low potassium it was found that if the potassium intake were raised from 1.6 gm. to 4 gm. there developed a prompt outpouring of sodium and chloride in the urine, the serum sodium fell and symptoms of crisis developed which required active treatment with cortin and intravenous salt.

Comparable increases in the potassium intake do not cause any marked change in the serum sodium in normal persons, though if the intake of sodium is high, administration of potassium salts may be followed by some increased urinary excretion of sodium. The action of the natural cortical hormone is apparently protective. Within what limits the administration of cortin will protect against the action of potassium in Addison's disease is not yet fully determined.

Wilder has pointed out that the normal diet contains variable amounts of potassium, many common foods such as meat, fish, potatoes, etc. yielding as much as 400 mg. per 100 gm. It is entirely possible, therefore, that an accidentally increased intake of potassium in the diet may account for some of the hitherto unexplained crises of patients under treatment with a high sodium intake alone. It would seem important therefore to add to the requirements for successful treatment of Addison's disease that dietetic measures be taken to ensure a potassium intake of not more than 1.6 gm. a day.

REVIEWS

The Diagnosis and Treatment of Variations in Blood Pressure and Nephritis. By HERMAN O. MOSENTHAL, M.D. 616 pages; 15.5 × 24 cm. Oxford University Press, N. Y. 1930, 1931. Price, $9.00.

This volume is divided into two parts, the first dealing with blood pressure and the second with nephritis. In the first part the physiologic dynamics controlling blood pressure, methods of estimating arterial tension, tests for functional efficiency of the circulation, blood pressure as applied to life insurance, the effects of certain everyday habits and daily routine upon the blood pressure, hypotension and hypertension are discussed. The author points out that moderately elevated blood pressures remaining at the same level do not have the same significance as those which progressively become higher. He classifies cases of hypertension according to the elevation of the systolic or diastolic pressure or both, and attributes the first to a large pulse volume or to a general rigidity of the arterial wall, the second to an associated myocardial insufficiency, the last to a primary increased peripheral vaso-constriction or more commonly to an increase in the tone of the arteries between the heart and arterioles with secondary arteriolar constriction—the cases in this latter group being considered those known as essential hypertension. In regard to the severity of the vascular lesions secondary to or associated with hypertension, the author points out the present confusion in the use of the terms benign and malignant and suggests that better terms would be "mild," "progressive," or "severe." The etiology, symptomatology and treatment of essential hypertension are discussed.

The second part of this volume is devoted to what the author prefers to call Bright's disease, since he feels that nephritis can no longer be considered a disease of the kidney alone, and since furthermore certain conditions included in the non-suppurative renal diseases are not inflammatory in origin. Included in this portion of the book is a discussion of the various types of pathological lesions found, methods of testing renal function, symptoms and signs of impaired function, and treatment. The author has divided treatment into that directed at the pathological lesion and that directed at the symptoms and signs exhibited by the patient. He stresses the point that each patient presents an individual problem. There are separate chapters on edema, anemia, blood pressure and uremia. A classification is offered.

Drs. Daniel R. Barr, Ernst P. Boas, Harold M. Frost, C. Ward Crampton, Edward C. Schneider, Benjamin I. Ashe, S. Edward King, and James J. Short have made contributions to this volume. There is an extensive bibliography.

W. S. L., JR.

Synopsis of Diseases of the Heart and Arteries. By GEORGE R. HERRMANN, M.D., Ph.D. 344 pages; 13 × 20 cm. C. V. Mosby Company, St. Louis. 1936.

This synopsis of cardiovascular disorders is intended for the student and general practitioner. It contains no reference lists but from time to time the names of outstanding investigators are mentioned in the text. It is well indexed. It contains chapters on modern instruments used in the clinical study of the heart, cardiologic roentgenology, and electrocardiography. This book is recommended to those wishing more information on this subject than is to be found in the textbooks on general medicine, and who do not wish to purchase or who have not the time to read one of the more extensive treatises on cardiovascular diseases.

W. S. L., JR.

The Medical Treatment of Gall Bladder Disease. By MARTIN E. REHFUSS, M.D., and GUY M. NELSON, M.D. 465 pages; 15 × 24 cm. W. B. Saunders Company, Philadelphia. 1935. Price, $5.50.

Any comprehensive presentation of the medical treatment of gall bladder disease is timely, for today the results of even expert surgery are often discouraging. Moreover, the mechanism of gall bladder disease is not reversed or changed by surgical treatment; such treatment merely removes the result of a pathological process without affecting its cause. In the light of our present knowledge Rehfuss and Nelson feel that like the diabetic, the chronic biliary sufferer needs an adjustment of his method of living, a recognition of certain dietary procedures, and equally important, a systematic check-up of his condition.

The book is well arranged and proceeds in orderly fashion first by stating the problem and then the methods whereby it may be attacked. The physiology of gall bladder activity is reviewed briefly. The important points in the clinical study of the gall bladder patient are described.

The authors believe that the primary problem in the treatment of gall bladder disease is a medical one, although surgical therapy is often necessary as a part of the general program. Certain cases they consider clearly candidates for surgery, but on the other hand they point out that there are exceptions to the rule that gall stones in themselves are an indication for surgical treatment. Careful consideration of the patient's status as a surgical risk is necessary. The clinical similarity to gall bladder disease of pancreatitis, appendicitis, and coronary disease should lead to a careful analysis of clinical data in each case before a final decision is reached.

In discussing the medical treatment, the authors stress the value of considering that in each patient with gall bladder disease one or more etiologic factors are chiefly at play and must be especially combated. The three major etiologic factors they consider to be metabolic defects, infections, and stasis. Diet regulation, the removal of focal infections, the use of vaccines, the employment of duodenal drainage, etc. are more or less appropriate therapeutic methods according to the etiologic factor which predominates in the individual case.

There is a very full discussion of diets, drugs, and special therapeutic methods. General hygiene, rest, exercise, work and diversion are considered from the point of view of the gall bladder patient.

S. M.

The Stomach and Duodenum. By GEORGE B. EUSTERMAN, and DONALD C. BALFOUR. 958 pages; 17 × 25 cm. W. B. Saunders Company. 1935. Price, $10.00.

This book is an excellent example of a coöperative effort on the part of competent men working in unison for the benefit of all of us. They supplement each others' knowledge and in that way are able to present the fundamental facts of diseases of the stomach and duodenum as well as their relationship to other diseases. The gastro-duodenal field is surveyed and brought up to date from all points of view, medical, surgical, physiological, pathological and roentgenological, and the result is an excellent book for internist, surgeon, general practitioner and student.

The authors and contributors have endeavored to confine their discussions to such phases as have more or less direct clinical application, and thus to emphasize the real purpose of coördinated practice, namely, that the benefit of all knowledge, whether clinical, experimental, surgical or pathological, be made available to the individual patient. They have omitted mention of conditions, anomalies, or therapeutic procedures with which they are not sufficiently familiar to cause their opinion to have weight, but on the other hand they have paid the greatest attention to diseases of frequent occurrence such as duodenal ulcer, gastric ulcer, dyspepsia, gastritis, hemorrhage, nutritional disorders, vitamin deficiency states, etc.

The first five chapters may be looked upon as reviews from the historical, physiological, experimental, surgical pathological and pathological points of view. They give the reader that fundamental knowledge upon which a satisfactory clinical approach can be substantially based. The general problem of dyspepsia is classified into four groups. These are the organic, reflex, systemic and functional. Then follows the investigation of the patient. Test meals are discussed and their diagnostic significance evaluated. An illustrated chapter is devoted to roentgenologic diagnosis. Anesthesia for surgical procedures involving the stomach and duodenum are duly considered.

The chapters on duodenal ulcer are excellent. Other phases of duodenal disease such as duodenitis, malignant and non-malignant tumors of the duodenum, tuberculosis of the duodenum, chronic dilatation and obstruction of the duodenum, fistulas and injuries of the duodenum, duodenal parasites, diverticula, paraduodenal hernia are considered. Gastric diseases are similarly discussed and it is interesting to see that the subject of gastritis is still a controversial one. Gastric ulcer and cancer, as would be expected, consume many pages. In the chapter on surgical treatment of carcinoma of the stomach, excellent step by step illustrations of various operative procedures are included. The importance of early diagnosis is stressed and the possibility of more and more five year cures is shown to depend upon early diagnosis, proper surgical technic and proper pre- and postoperative care of the patient.

Achlorhydria assumes added significance in view of recent advances in the understanding of it. A chapter is devoted to the medical treatment of inoperable carcinoma of the stomach, a subject upon which we always need enlightenment. The subject of diaphragmatic hernia is discussed. Apparently what was interpreted as an increase in its incidence is due entirely to the awareness that the condition exists and to better diagnosis.

The important subjects of perforation and hemorrhage and their treatments as well as the problem of gastric retention due to duodenal and pyloric obstruction are considered thoroughly. A chapter is also devoted to that moot question of carcinomatous transition of gastric ulcer and another to anemia following operations on the stomach.

It is apparent, therefore, that we have here perhaps the most complete treatise on the stomach and duodenum in the English language. The work is systematically and skillfully arranged following a plan which devotes one-third of the book to general and fundamental considerations, one-third to a discussion of the duodenum in practically all its phases and the final one-third to a similar discussion of the stomach, except for the last chapter which discusses the nature of postoperative pulmonary disease. Both stomach and duodenum are considered in the same sequence.

The bibliography is selective, comprehensive and authoritative. The illustrations are splendid. The book can be highly recommended. S. M.

Lobar Pneumonia and Serum Therapy. By FREDERICK T. LORD, M.D., and RODERICK HEFFRON, M.D. 91 pages. The Commonwealth Fund, New York. 1936. Price, $1.00.

This small book, written with special reference to the experience of the Massachusetts Pneumonia Study, will be of interest and value to all those engaged in the care of pneumonia cases. It deals first with the underlying immunological problems and then in a very practical and specific way with such topics as the selection of cases for serum treatment, the technic of typing, the methods and precautions useful in serum therapy, dosage, and reactions. In the last chapter new data are added concerning the results of serum therapy.

The presentation will be clear to any intelligent practitioner and at the same time the observations recorded will be valuable to those fully conversant with the previous literature of this subject. M. C. P.

COLLEGE NEWS NOTES

Gifts to the College Library

Acknowledgment is made of the receipt of the following gifts to the library of the American College of Physicians:

Dr. Oliver T. Osborne (Fellow), New Haven, Conn.—3 books, "What Everyone Ought to Know," "Mouth Infection" and "Evaluation of Symptoms";
Dr. Jacob Gutman (Fellow), Brooklyn, N. Y.—Sixth Supplement to his book, "New Modern Drugs," previously donated to the College;
Dr. Jacob Buckstein, New York, N. Y.—1 book, "Peptic Ulcer";
Lt. Col. Thomas W. Burnett (Fellow), M.C., U. S. A.—1 reprint;
Dr. Arthur R. Elliott (Fellow), Chicago, Ill.—18 reprints;
Dr. Hubert C. King (Fellow), Lakewood, Ohio—1 reprint;
Dr. E. B. Krumbhaar (Fellow), Philadelphia, Pa.—16 reprints;
Dr. Albert Soiland (Fellow), Los Angeles, Calif.—6 reprints;
Dr. Pauline Williams (Fellow), Richmond, Va.—2 reprints;
Dr. W. Lawrence Cahall (Associate), Philadelphia, Pa.—1 reprint;
Dr. Richard J. Clark (Associate), Boston, Mass.—3 reprints;
Capt. James H. Forsee (Associate), M.C., U. S. A.—5 reprints;
Dr. William Freeman (Associate), Worcester, Mass.—10 reprints;
Dr. Ralph H. Kuhns (Associate), Chicago, Ill.—1 reprint;
Dr. Fred J. McEwen (Associate), Wichita, Kan.—1 reprint;
Dr. G. Louis Weller, Jr. (Associate), Washington, D. C.—4 reprints;
Dr. F. Eugene Zemp (Associate), Columbia, S. C.—4 reprints.

The North Carolina State Medical Society met in Asheville May 4 to 6, under the presidency of Dr. Paul H. Ringer (Fellow), Asheville. A luncheon by North Carolina members of the American College of Physicians was given Tuesday, May 5, in honor of Dr. Ernest B. Bradley, President of the College, at which 36 Fellows out of a State membership of 66 were present. In addition to President Ringer, four ex-Presidents of the State Society were present, Dr. L. B. McBrayer, Southern Pines; Dr. M. L. Stevens, Asheville; Dr. Isaac Manning, Chapel Hill; and Dr. Paul P. McCain, Sanatorium, as well as Dr. Wingate M. Johnson, Winston-Salem, President-Elect of the Society, all Fellows of the College. Dr. Bradley spoke briefly explaining the progress of the Committee on the Certification of Internists.

Under the Presidency of Dr. James E. Paullin (Fellow), the Medical Association of Georgia recently held its 87th Annual Session. Dr. William B. Castle (Fellow), recipient of the Phillips Memorial Award of the American College of Physicians for 1933, delivered the Abner Wellborn Calhoun Lecture.

Dr. J. Frederick Painton (Fellow), Buffalo, N. Y., has been appointed Associate in Medicine at the University of Buffalo School of Medicine for the academic year, 1936 to 1937.

Dr. A. U. Desjardins (Fellow) Rochester, Minn., is Chairman of the American committee in charge of the First International Congress on Fever Therapy to be held at Columbia University, New York City, September 29 to October 3, 1936. The subjects to be discussed will include physiologic and pathologic changes as well as the

treatment of gonorrhea, both in the male and in the female; gonorrheal and non-specific arthritis; syphilis in its various stages; neurologic conditions such as multiple sclerosis, chorea, paresis, tabes; skin diseases, etc. This meeting will be held under the Chairmanship of Baron Henri de Rothschild of Paris, France. There is a French committee headed by Professor d'Arsonval as honorary President and Professor Abrami as Chairman. There is a national European committee with members representing various European countries.

An abstract of the papers will be published in the volume of the transactions in English, German and French. Information regarding the conference may be obtained from the Secretary, Dr. William Bierman, 471 Park Avenue, New York, N. Y.

Dr. William Nimeh (Fellow), Mexico, D. F., has been elected President of the Mexican Chapter of the National Society for the Advancement of Gastro-enterology.

Dr. Nimeh also was recently and unanimously elected a member of the National Academy of Science.

Dr. Archibald L. Hoyne (Fellow), Clinical Professor of Pediatrics, Rush Medical College, and Associate Clinical Professor of Pediatrics, School of Medicine of the Division of the Biological Sciences, University of Chicago, addressed the Northern Tri-State Medical Meeting at Fort Wayne, Ind., in April on "Progress in the Management of Contagious Diseases."

He also addressed the Nebraska State Medical Meeting at Lincoln, during April, on "The Treatment of Meningococcic Meningitis Without Intraspinal Therapy," and the Iowa Public Health Association's meeting at Des Moines, on April 28, on "Diphtheria." On May 29 he addressed the Iowa State Medical Meeting at Des Moines on "Meningococcic Meningitis."

Dr. C. C. Burlingame (Fellow), Hartford, Conn., as Chairman of the Committee on Public Education of the American Psychiatric Association, recently announced the election by the Board of Examiners of that organization, of Dr. Kenneth Appel (Associate), Philadelphia, Pa.

Dr. Howard M. Jamieson (Fellow), Wilkes-Barre, Pa., has accepted a Public Health appointment in Great Britain.

Newly elected Fellows of the American College of Physicians of Puerto Rico gave a dinner on April 28 in honor of the College Governor of the Island, Dr. R. M. Suarez. Dr. Suarez presented a report upon the Twentieth Annual Session of the College held in Detroit, at which he was in attendance. There was a round table discussion in regard to the College, its policies and the further development of its membership in Puerto Rico. Action was taken toward organizing a local unit with the purpose of furthering the aims and objects of the College and its scientific activities in the Island.

Under the Presidency of Dr. F. M. Pottenger (Fellow), Monrovia, the Twentieth Annual Scientific Session of the Association for the Study of Internal Secretions was held in Kansas City, May 11 to 12. Among members taking part in the program were:

Dr. E. L. Sevringhaus (Fellow), Madison, Wis. (with R. K. Meyer)—"Gonadotropic Inhibitory Substances in Blood of Women and Monkeys After Anterior Pituitary Therapy";

Dr. J. B. Collip (Fellow), Montreal, Que. (with Hector Mortimer, Percy Wright, Carl Bachman)—"The Hormone Relationship Between the Female Organs of Sex and the Nasal Mucous Membrane" and "Further Studies in Anterior Pituitary Physiology";

Dr. Henry J. John (Fellow), Cleveland, Ohio—"The Interrelationship Between the Pancreas and Other Endocrine Organs in Diabetes";

Dr. Hans Lisser (Fellow), San Francisco, Calif.—"Two and One-Half Years' Observation of a Patient with Cushing's Disease, Following Removal of a Pars Intermedia Adenoma";

Dr. W. O. Thompson (Fellow), Chicago, Ill. (with N. J. Heckel, A. D. Bevan, E. R. McCarthy and P. K. Thompson)—"The Treatment of Undescended Testicles with an Anterior Pituitary-Like Substance";

Dr. L. G. Rowntree (Fellow), Dr. J. H. Clark (Fellow) and Dr. N. H. Einhorn (Fellow), all of Philadelphia (with Arthur Steinberg, Philadelphia, and A. M. Hanson, Faribault, Minn.)—"The Rôle of the Thymus Gland in Growth and Development";

Dr. Homer P. Rush (Fellow), Portland, Ore.—"Three Cases of Macrogenitosomia";

Dr. Daniel L. Sexton (Fellow), St. Louis, Mo.—"Treatment of Sexual Underdevelopment in the Human Male with Pregnancy Urine Extract. Further Report";

Dr. Matthew Molitch (Associate), Jamesburg, N. J. (with Sam Poliakoff)—"Hypothyroidism in Behavior Problems."

Dr. Joseph C. Doane (Fellow), Medical Director of the Jewish Hospital of Philadelphia, will give a short course in hospital operation in the Summer School of Hotel Administration at Cornell University, June 29 to July 11. The course, planned as a "refresher" course for those already engaged in hospital work, is a "unit" course, which means that students enrolled will devote all their study time exclusively to the study of hospital problems.

The Philadelphia County Medical Society, during the week of April 20, 1936, conducted its First Annual Postgraduate Institute. Authorities in their respective fields offered postgraduate lectures relating especially to cardiovascular and renal diseases. Admission was open to all interested physicians not only locally but throughout the eastern portion of the country. The following Fellows of the College were members of the Committee on the Postgraduate Institute: Dr. E. J. G. Beardsley, Dr. Edward L. Bortz, Dr. Willis F. Manges, Dr. H. K. Mohler and Dr. William D. Stroud.

Dr. David P. Barr (Fellow) and Dr. Sinclair Luton (Fellow), both of St. Louis, addressed the annual meeting of the Missouri State Medical Association at Columbia, Mo., on "Nature and Treatment of Obesity" and "The Clinical Use of Digitalis: Variables Encountered," respectively.

Dr. William Devitt (Fellow), Allenwood, Pa., is President of the Pennsylvania Tuberculosis Society, succeeding Dr. Charles Howard Marcy (Fellow), Pittsburgh.

Under the Presidency of Dr. Herbert L. Bryans (Fellow), Pensacola, the 63rd Annual Meeting of the Florida Medical Association was held on the S. S. Florida, April 27 to 29, on a cruise to Havana.

Dr. Willis F. Manges (Fellow), Philadelphia, presented the Russell D. Carman Memorial Lecture, sponsored by the Minnesota Radiological Society, during the annual session of the Minnesota State Medical Association at Rochester, Minn., early in May. Dr. Manges' title was "Foreign Bodies and the Use of X-Ray Examination in Their Localization and Removal."

Dr. James Alex. Miller (Fellow) has been appointed Administrative Consultant in Tuberculosis to the New York City Department of Hospitals.

A reception and testimonial dinner was tendered to Dr. Andrew P. Biddle (Fellow), Detroit, on April 1 by the Wayne County Medical Society and the Detroit Dermatological Society in recognition of his completion of fifty years in the practice of medicine. Dr. Biddle is Emeritus Professor of Dermatology at Wayne University, College of Medicine. He was President of the Detroit Board of Education in 1925, President of the Detroit Library Commission in 1931, Charter member of the Wayne County Medical Society and was the first Editor of the Journal of the Michigan State Medical Society. He has also acted as President of the State Society, President of the Detroit Academy of Medicine and President of the American Dermatological Society.

Dr. Robinson Bosworth (Fellow), Rockford, has been elected President of the Illinois Tuberculosis Society.

Dr. Andrew C. Ivy (Fellow), Chicago, has been named Secretary of the American Physiological Society.

Under the Presidency of Dr. Robert A. Peers (Fellow), Colfax, Calif., the 65th annual meeting of the California Medical Association was held at Coronado, May 25 to 28. Dr. Jacob J. Singer, St. Louis, Dr. Harry H. Wilson, Los Angeles, Dr. F. M. Pottenger, Monrovia, Dr. Philip H. Pierson, San Francisco, all Fellows of the College, were among the speakers on the program.

Dr. Ralph A. Kinsella (Fellow), St. Louis, delivered the annual oration in medicine before the Illinois State Medical Society at its meeting in Springfield, May 19, his title being "The Career of a Heart."

Dr. George W. Covey (Fellow), Lincoln, Nebr., was installed as President of the Nebraska Medical Association at its 68th annual meeting during April.

Dr. Peter Irving (Fellow), New York City, is Secretary of the Medical Society of the State of New York.

Dr. Earl B. McKinley (Fellow), Washington, D. C., has been named Vice-President of the American Association of Pathologists and Bacteriologists.

Dr. Charles F. Martin (Master) for many years Dean of the Faculty of Medicine of McGill University, Montreal, will retire August 31, having reached the retirement age in effect at that institution.

Dr. Albert Grant Fleming, Professor of Public Health and Preventive Medicine and Director of the Department, has been appointed Dean to succeed Dr. Martin.

A newly established position of Associate Dean will be filled by J. C. Simpson, LL.D., Secretary of the Faculty of Medicine and Chairman of the Committee on Physical Education.

OBITUARIES

DR. CLARENCE EUGENE SIMONDS

Clarence E. Simonds was born February 13, 1874, in the town of Mansfield, Conn., a son of William E. and Mary (Lee) Simonds.

He was educated in the common schools of Mansfield and graduated from Willimantic High School in 1893. After teaching for a year he entered the medical school of New York University, finishing the course there in 1897. Following this he did postgraduate work at New York Postgraduate Medical School and Hospital.

He practised his profession in Danielson and South Coventry, Conn., before beginning to practice in Willimantic in 1903, where he has remained until about a year ago when failing health caused him to give up all active work. He served as health officer of the town of Windham and was medical examiner for the towns of Windham, Scotland and Hampton for many years until ill health compelled him to resign.

He was formerly Attending Physician, St. Joseph's Hospital, Chief Physician and President of the Medical and Surgical Staffs, Windham Community Memorial Hospital, ex-president and ex-secretary of Willimantic City Medical Society, ex-president of Windham County Medical Society, a member of the Connecticut State Medical Society and of the American Medical Association. He was also a member of the Willimantic Chamber of Commerce and past president of the Exchange Club. He became a Fellow of the American College of Physicians in 1930.

At the time of his death he was president of the professional staff of the Windham Community Memorial Hospital.

HENRY F. STOLL, M.D., F.A.C.P.,
Governor for Connecticut

DR. ARTHUR D. HOLMES

Arthur David Holmes, M.D., C.M., Detroit, Michigan, died after a short illness, February 20, 1936.

Dr. Holmes was born in Chatham, Ontario, in 1863. He graduated from McGill University, Faculty of Medicine, in 1889, and then started practice in Detroit. Very early he confined his work to pediatrics. He spent the year 1902–1903 in London and Vienna doing graduate work in the diseases of children.

He held numerous teaching and hospital appointments: Attending Physician, Children's Free Hospital, 1905–1916; Attending Physician, Woman's

Hospital and Infants' Home, 1907–1916; Consultant to both of these institutions to the time of his death; Clinical Professor of Pediatrics, Detroit College of Medicine, 1913–1916. He held membership and office in many medical societies: Wayne County Medical Society (President in 1910, and a Trustee from 1910 to 1930); Michigan State Medical Society; American Medical Association; Detroit Acadmey of Medicine (President, 1901); Mississippi Valley Medical Association (Vice-President, 1912); Central States Pediatric Society. Dr. Holmes was one of the very early members of the American College of Physicians, having taken Fellowship in 1917. He was also a Director of the Equitable Trust Company, Charles W. Warren Company, and the Central West Casualty Company. In social organizations he held membership in the Detroit Club, the Witenagemote Club, and the Detroit Country Club.

Dr. Holmes had been a widower for many years, and is survived by two daughters, Mrs. Ernest G. Davis and Miss Agnes Holmes of Detroit.

Dr. Holmes' death is a great loss to the medical profession of the city and state. He was one of the earliest to confine his work to pediatrics, and for many years was an active teacher in the college and hospitals of the city. As an able clinical teacher, his work became the inspiration for many of our younger pediatricians. A gentleman of broad culture and great personal charm, he enjoyed a wide social acquaintanceship in the city. Organized medicine also owes a great debt to Dr. Holmes, for it was during his presidency in 1910 and under his inspiring guidance, that the Wayne County Medical Society first purchased and became quartered in a building of its own, marking an important step in the growth and prosperity of the Society. The profession will miss greatly his genial friendship, and his able professional counsel.

HENRY R. CARSTENS, M.D., F.A.C.P.,
Governor for Michigan

DR. WEBSTER STANLEY SMITH

Dr. Webster Stanley Smith (Associate), Dayton, Ohio, died January 30, 1936, of arteriosclerosis, at the age of 79. Dr. Smith was born in Dayton, November 13, 1856. He attended the public schools and graduated from the Medical College of Ohio in 1880. For many years he was connected with the Miami Valley Hospital as a member of the department of medicine and as instructor to nurses in diseases of the chest. He was a member and past president of the Montgomery County Medical Society; a member of the Ohio State Medical Society, the Mississippi Valley Medical Society, the American Medical Association, and had been an Associate of the American College of Physicians since 1925.

MINUTES OF THE BOARD OF REGENTS

DETROIT, MICH.

March 1, 1936

A regular meeting of the Board of Regents was held at the Book-Cadillac Hotel, Detroit, March 1, 1936, with the following present: James Alex. Miller, President; Ernest B. Bradley, President-Elect; David P. Barr, Second Vice-President; William Gerry Morgan, Secretary-General; William D. Stroud, Treasurer; Walter L. Bierring, John H. Musser, O. H. Perry Pepper, Francis M. Pottenger, Luther F. Warren, William J. Kerr, Roger I. Lee, Sydney R. Miller, George Morris Piersol, G. Gill Richards, James B. Herrick, Jonathan C. Meakins, James H. Means, James E. Paullin, Maurice C. Pincoffs, Charles H. Cocke, and Dr. Alfred Stengel, Chairman, College Headquarters Committee, and Mr. E. R. Loveland, Executive Secretary, acting as secretary of the meeting; with Dr. James Alex. Miller, of New York City, President of the College, presiding.

The Executive Secretary read abstracted Minutes of the meeting of the Board of Regents held in Philadelphia December 15, 1935, which were approved as read.

President Miller in preliminary remarks referred with regret to the death of Dr. Charles G. Jennings, General Chairman of the Twentieth Annual Session; to two main subjects to be discussed later in the meeting, namely, the matter of a permanent home for the College and the certification of internists by the American Board of Internal Medicine; and to the remarkably satisfactory manner in which the Executive Offices had functioned during the past year.

The Executive Secretary then presented a communication from Professor M. Fernán-Núñez of Marquette University School of Medicine, Milwaukee, inviting, on behalf of Prof. Dr. Gustavo Pittaluga, Madrid, Spain, President of the III International Congress on Malaria to be held there October 12 to 18, 1936, some representative of the College to attend the Congress.

On motion by Dr. Bierring, seconded by Dr. Pepper, and regularly carried, it was

RESOLVED, that the incoming President, Dr. Ernest B. Bradley, may designate any Fellow of the College whom he finds is going to attend this Congress to act as the official delegate of the American College of Physicians.

Dr. Ernest B. Bradley, Chairman of the Committee on Public Relations, presented the following resignations, which were acted upon by resolution:

Associates

Bernard G. Efron	New Orleans, La.
Walter S. Lucas	Wynnewood, Pa.
Jenaro Suarez	San Juan, P. R.

Fellows

W. L. Holman	Toronto, Ont.
Lester J. Williams	Baton Rouge, La.

RESOLVED, that the resignations of the three above named Associates and two Fellows be accepted.

Dr. William Gerry Morgan, Secretary-General, presented the following resolution, which was unanimously adopted, on the death of Dr. Charles G. Jennings (Master), including its being spread upon the Minutes of this meeting and a copy of it being sent to Dr. Jennings' son, Dr. Alpheus Jennings.

IN MEMORIAM

CHARLES GODWIN JENNINGS

WHEREAS: Through the death of Charles Godwin Jennings on January 9th, 1936, the American College of Physicians has lost one of its earliest and most distinguished members.

Dr. Jennings was elected to Fellowship in 1916 at the first annual meeting of the College held in New York City. He was the second Fellow to be elected Master.

During the twenty years of his membership as Fellow and Master, Dr. Jennings took an active part in shaping the development of the College.

He was President of the American Congress on Internal Medicine 1925 to 1926, at that time an integral part of the College. He served for many years as Governor of the College for the State of Michigan, and as such built up a large and enthusiastic State membership. On his retirement from the office of Governor, he was elected to the Board of Regents and served in this capacity until 1930. He was elected Second Vice-President of the College in 1931 and served until 1933, when he was made First Vice-President. Dr. Jennings was returned to the Board of Regents in 1935 for a term of three years.

At the time of his death, Dr. Jennings was General Chairman for the Twentieth Annual Meeting of the College.

Dr. Jennings by his broad vision, keen judgment and wise counsel had won the confidence and esteem of those with whom he had worked for so many years.

THEREFORE BE IT RESOLVED: that we express our deep sorrow for the loss of this true physician and wise counselor.

The Executive Secretary, Mr. Loveland, presented cases of failure to take up election, delinquency, and failures to qualify for Fellowship. Two names were discontinued on the Fellowship Roster for failure to take up election; 14 Associates were dropped from the roll for failure to qualify for Fellowship within five years of their election to Associateship, as required by the By-Laws; 7 Fellows and 5 Associates were dropped from the roll because of delinquency of two years or more.

Reporting upon the candidates elected to Associateship in 1931 and whose term of Associateship expires with the 1936 Annual Session, the Executive Secretary presented the following analysis:

78 Qualified for Fellowship
2 Died
4 Resigned
1 Failed to take up election
16 Were rejected or dropped

101 Total elected 1931

77.2% qualified for Fellowship; 22.8% failed ever to become Fellows.

Dr. William Gerry Morgan, Secretary-General, reported the deaths of the following members since the last meeting of the Board of Regents:

Master		
Charles Godwin Jennings	Detroit, Mich.	January 9, 1936
Fellows		
Henry Wald Bettmann	Cincinnati, Ohio	December 5, 1935
Thomas C. Chalmers	Forest Hills, N. Y.	November 16, 1935
William Krauss	Meridian, Miss.	December 21, 1935
George Washington McCaskey	Fort Wayne, Ind.	December 30, 1935
Stephen Roman Pietrowicz	Chicago, Ill.	January 12, 1936
Hubert Schoonmaker	Clifton Springs, N. Y.	October 21, 1935
Charles D. Steinwinder	San Antonio, Tex.	
Associates		
John Leonard Eckel	Buffalo, N. Y.	November 26, 1935
Henry Finlay Hyndman	Wichita, Kan.	October 31, 1935

Dr. Morgan also reported the following list of Fellows who have become Life Members since the last meeting of the Board of Regents. This made a total of sixty-one Life Members, including the late Dr. John Phillips.

Lewis Beals Bates	Ancon, Canal Zone
Casper H. Benson	Columbus, Ohio
Donald Gregg	Wellesley, Mass.
James Rae Arneill	Denver, Colo.
Thomas Fitz-Hugh, Jr.	Philadelphia, Pa.
C. Charles Burlingame	Hartford, Conn.
Noble Wiley Jones	Portland, Ore.
Cecil M. Jack	Decatur, Ill.
Anna Weld	Rockford, Ill.
Roy M. Van Wart	Descanso, Calif. (formerly of New Orleans)
Estes Nichols	Portland, Maine
William Henry Watters	Coconut Grove, Miami, Fla.

Dr. George Morris Piersol, Chairman of the Committee on Credentials, reported that the Committee had held two meetings, one at the College Headquarters in Philadelphia on February 2 and one at Detroit on March 1. He distributed to the Board of Regents a mimeographed list of the recommendations for election both to Fellowship and Associateship from the meeting of February 2. An analysis of this list follows:

Recommended for election to Fellowship:	
Advancement for Associateship	39
Direct election to Fellowship	15
	54
Recommended for election to Associateship first	1
Deferred for further investigation, maturity, etc.	10
Rejected	1
	66

Of those recommended for election directly to Fellowship, the majority were members of the Medical Corps of the U. S. Army and U. S. Navy.

An analysis of the recommendations of the Committee on the Associate candidates considered February 2 was as follows:

Recommended for election to Associateship:	
From regular list	48
From Fellowship list	1
	49
Deferred for further consideration	11
Rejected	6
	66

Dr. Piersol having insufficient time to mimeograph the recommendations of March 1, read the list of recommendations to the Board. His analysis of the candidates considered on March 1 was as follows:

Recommended for election to Fellowship:	
Advancement from Associateship	40
Direct elections to Fellowship	11
	51
Recommended for election to Associateship first	1
Deferred for further investigation, maturity, etc.	4
Rejected	3
	59

An analysis of the candidates considered for Associateship on March 1, follows:

Recommended for election to Associateship	41
Recommended for election directly to Fellowship	2
Deferred for further consideration	2
Rejected	7
	52

The combined lists of recommendations from the meetings of February 2 and March 1, both for Fellowship and Associateship, follow. On motion by Dr. Piersol, seconded by Dr. Bradley and regularly carried, it was

RESOLVED, that the following 105 candidates for Fellowship and 92 candidates for Associateship shall be and are hereby elected to membership in the respective classes indicated.

The complete list of elections was published in the March, 1936, issue of this journal.

Dr. Piersol, on behalf of the Committee on Credentials, presented two cases for advice and direction from the Board of Regents: (1) the case of a Fellow who resigned some years ago and who now is interested in being reinstated, but at a minimum of expenditure. After thorough discussion of the case, the Board of Regents, by resolution, directed that it shall be the policy in such cases to require the payment of all delinquent dues and to have the support and recommendation of the Governor of the district for reinstatement. The Board expressed itself as unfavorable to establishing a precedent of permitting members to leave and reënter the College at will without any obligation in the meantime. The only other method of regaining membership would be through an original proposal and reëntry according to the present requirements; (2) the case of a former Fellow who subsequently became a Fellow of the American College of Surgeons and who specialized thereafter particularly in Obstetrics, although he is highly accomplished also in Internal Medicine. This member had resigned his Fellowship in the American College of Physicians because he understood it was the policy of the College not to include in its membership those engaged in obstetrical practice, or those who had become members also of the American College of Surgeons. This case was presented to determine whether the Board of Regents would consider reinstatement to active Fellowship in this College. A resolution was adopted re-

iterating the fact that the policy of the American College of Physicians remains the same in this respect as in the past, and that consequently as long as the candidate in question remains a Fellow of the American College of Surgeons and is not confining his work mainly if not exclusively, to Internal Medicine, the case cannot be reopened.

Dr. Alfred Stengel, Chairman of the temporary Committee on the College Headquarters, reported that after his Committee had considered the matter, it had come to the conclusion that it was of such importance that the broad question of principle should be passed upon by the Regents before the Committee engaged anyone to draw up detailed plans. Therefore, he reported only upon the general proposition of a College Headquarters. There were two problems: first, whether the College wishes or requires a building for its headquarters, leaving rental considerations altogether out of mind; and, second, if they do feel that they should have such a building or headquarters, how far the Board of Regents of the College would like to go in the matter of expenditure. In regard to the question of the desirability, it has been the feeling of all the members of the Committee, perhaps with some slight amendment in the way it was presented, that it seems desirable that the College should have a dignified place wherever the headquarters of the College will be located, where Fellows of the College, as they may perhaps be going through that center, would find occasion to make visits either to obtain information, to arrange programs or to stop casually. He had obtained information from the Executive Secretary that aside from the meetings of the Regents and Governors at the College Headquarters, from time to time, there are perhaps one hundred and fifty or more visitors from the membership of the College every year who come to the headquarters for one purpose or another. The universal comment of visitors is that the College Headquarters is inadequate and inferior. He said there are all kinds of reasons that may be advanced as to why the College should have a central headquarters, but that he was passing over those to consider the question of finances. The Committee had determined that the cost of operating its headquarters, including the loss of interest on the investment, maintenance, light, heat, taxes, etc., would total about $8,000.00 per annum. This was all predicated on the erection of a building that would cost approximately $100,000.00. Calculating the amount of space that the Executive Offices reasonably would require in the building where they are now located, the cost would be approximately $7,800.00 per annum, or a difference only of $200.00 between offices in an ordinary office building and headquarters in a dignified, individual home.

Dr. Stengel reported that his Committee had surveyed many properties in the vicinity of the present College Headquarters, and had found one location, a vacant lot in a very desirable neighborhood, convenient to one of the large academic medical centers, to a first-class hotel and to transportation, which could be obtained for about $30,000.00. The Committee felt that an appropriate headquarters could be erected and furnished for an additional $70,000.00, as an outside figure. An architect, without charge to the College, had made several sketches and submitted different kinds of plans, making the estimate within the amount indicated above, and providing for materials of the best quality and a fireproof structure. Dr. Stengel described the architect's plans, which were presented purely as a working basis and a theoretical possibility, that called for a Georgian building of two stories with an unfinished third floor, of construction permitting for adding additional floors if in future years such would be required. The type of architecture was in keeping with the surrounding buildings.

The Committee recommended to the Board of Regents favorable consideration of a permanent headquarters building erected and furnished in Philadelphia at a cost not to exceed $100,000.00.

After wide discussion, a resolution was adopted to the effect that it was the sense of the Board of Regents that they approve in principle the program outlined by the Committee, but that final action be deferred until after a conference with the Board of Governors and until further and more specific details can be obtained.

Even after the adoption of this resolution, there was extended discussion in which it was brought out that the location considered was not far removed from the new main station

of the Pennsylvania Railroad and the new U. S. Post Office. The location was thought by some to be one that would be definitely appreciating in value as years go by.

The consensus of opinion was that the College should be conservative, should not expend an unnecessary amount, other than reasonably required, that it should take into consideration various uses for the College funds, but that if an approprate College Headquarters of dignified character and adequate facilities could be provided, it would be a tangible evidence of its existence, that it would be a convenience to its members, and would provide better facilities for the proper functioning of the Executive Offices.

The discussion led also to a consideration of the initiation fee for Fellowship, it being suggested that as soon as possible, the Board should take under consideration a reduction of the present initiation fee of $80.00. There has been an erroneous idea that the initiation fee was $100.00, to which the annual dues have to be added. As a matter of fact, the initiation fee is but $80.00 a year for practicing clinicians, with a gradual reduction, according to salary, for those employed as medical teachers or research workers in non-profit institutions.

At the end of the discussion, Dr. Stengel concluded with the following remarks:

"I have tried to present this matter as objectively as possible, without going into some of the details that have been brought forward. The College has accumulated funds at a fairly rapid rate, due in great measure to its careful administration. If you can now invest some of that money to house yourself and pay your own headquarters rent instead of leaving it invested in funds producing income which you might be spending in other ways, your situation will be exactly the same. You are going to spend the same amount of money for rental as you will be spending upon this new building. It leaves you just where you are.

"The second proposition that immediately suggests itself is that the College could afford to reduce its present initiation fee. One of my fears is, and I am speaking as an 'ex-,' is that the College will get too many members, which will kill it, and at present you are either right on the edge of or you have already accomplished a stricter method of surveillance of those who are candidates, which will keep out undesirables. If you had eliminated your initiation fee five years ago and persons could have come into the College without an initiation fee, but by merely paying $15.00 a year dues, you would have had a much louder outcry at your door for admission on the part of undesirables. Your Committee on Credentials would have had a much harder job, and no matter how hard they worked, they would have let in a lot more undesirables than they did let in. Your initiation fee, in a sense, has stood as a guardian for the College. Now, with the proposition of a strict examination for admission to the College, that reason for an initiation fee will no longer exist in the same manner, and I think that this proposition makes it entirely possible to take some of your surplus and put it into a building which will make for a sense of stability and a sense of dignity, rather than to be merely a showplace.

"In my earlier report I mentioned the number of people who stop at the headquarters. Although that is a very unimportant thing and no one, I would think, would regard it otherwise, yet when one hundred and fifty men come along and say with disappointment, 'Is this where you live?'—well, that is one hundred and fifty men in an organization who go away and tell a sundry other one hundred and fifty men what they think of it. There is no strong argument for putting up a palace, but I think a dignified building that lends a sense of stability to an organization is a very important thing, and I think that financially you can well afford to do it; and, after you have got it, you can well afford to reduce your initiation fee and, perhaps, other fees as well."

Dr. Walter L. Bierring, as Chairman of the joint Committee on the Certification of Internists, distributed copies of his report, which was as follows:

REPORT OF JOINT COMMITTEE

(American Board of Internal Medicine)

DETROIT, MICH.,
March 1, 1936

TO PRESIDENT JAMES ALEX. MILLER
AND
MEMBERS OF THE BOARD OF REGENTS,
AMERICAN COLLEGE OF PHYSICIANS:

Since the report of this Joint Committee presented to the Regents at the meeting in Philadelphia, December 15, 1935, the further developments in the formation of the American Board of Internal Medicine are reported herewith.

1. An application in due form was submitted to the Advisory Board for Medical Specialties, which functions in connection with the Council on Medical Education and Hospitals of the American Medical Association, for approval of the organization of the American Board of Internal Medicine.

This application was accompanied by a copy of the proposed Articles of Incorporation, which embodied the Constitution, a copy of the By-Laws, which includes the requirements and methods of Certification of Specialists in Internal Medicine and a copy of the application blank.

Within a short time, advice was received from Dr. Paul Titus, the Secretary of the Advisory Board for Medical Specialties, that its Committee on Credentials and Qualifications had reported favorably on the application and so recommended to the Executive Committee of the Advisory Board for its meeting in Chicago on February 16, 1936.

2. The Joint Committee met in Chicago on Sunday, February 16, 1936, at which time certain minor changes were made in the Articles of Incorporation and the By-Laws, which were then submitted in corrected form to the Executive Committee of the Advisory Board of Medical Specialties; members Irons, Middleton and Bierring appearing for the Joint Committee.

The Executive Committee of the Advisory Board approved the formation of the American Board of Internal Medicine and transmitted its action to the Council on Medical Education and Hospitals of the American Medical Association at its meeting on Monday, February 17, 1936, which Council endorsed the action of the Advisory Board.

It was stated by both of the above bodies that final official action and approval would be withheld until a meeting of the entire Advisory Board for Medical Specialties and that of the Council on Medical Education and Hospitals in Kansas City, Mo., May 10 to 15, 1936, during the annual session of the American Medical Association.

If the Regents of the American College of Physicians, during this session, can approve the steps thus far taken in the formation of the American Board of Internal Medicine, the further official approval of the Section on Practice of Medicine of the American Medical Association can be obtained at its executive meeting on May 15, 1936, at Kansas City. After this has been accomplished, all the requirements of organization will have been complied with and the American Board of Internal Medicine will then be ready to begin operations.

At the meetings in Chicago, February 16 and 17, 1936, the Advisory Board for Medical Specialties and the Council directed that the Articles of Incorporation be filed in a Court of Record and this was accordingly done at Des Moines (Polk County), Iowa, on Friday, February 28, 1936.

The three required witnesses to the document, residents of Des Moines, were Dr. Tom B. Throckmorton, Governor for Iowa of the American College of Physicians, Dr. Fred Moore, Member, Council on Medical Education and Hospitals of the American Medical Association, and Dr. Walter L. Bierring, Member of the Joint Committee.

The purpose of filing these Articles in Iowa seemed advisable because of more favorable regulations in this State for non-profit sharing corporations. A special filing fee, an annual report and registration are not required as is the custom in some of the other States.

Because the Articles are filed in Iowa does not imply that the place of business of the Board shall necessarily be in Iowa.

It will be noted by the accompanying copy of the Articles of Incorporation (Constitution), that the American Board of Internal Medicine is composed of nine members, five of which shall be Fellows of the American College of Physicians, and four shall be representative of the Section on Practice of Medicine of the American Medical Association.

Previous to the meeting of the Advisory Board for Medical Specialties in Chicago on February 16, 1936, Dr. James Alex. Miller, by virtue of his authority as President of the American College of Physicians, submitted to the secretary of the Advisory Board, Dr. Paul Titus, the names of Drs. Meakins, Pepper, Middleton, Barr and Richards to represent the American College of Physicians, and in like manner, Dr. William J. Kerr, as Chairman of the Section on Practice of Medicine of the American Medical Association, the names of Drs. Fitz, Irons, Musser and Bierring to be members of the first American Board of Internal Medicine.

The By-Laws include the requirements for special training in Internal Medicine and procedure of Certification, which incorporate the report of the special committee appointed at the meeting on December 14, 1935—Drs. Meakins, Fitz, Irons and Middleton.

The Founders Group or Charter Members which are to be certified without examination within the period until July 1, 1937, will be more limited in number than at first proposed.

The Joint Committee expects to hold a meeting tomorrow, Monday, March 2, 1936, at 4:00 p.m., at which time further details of organization of the American Board of Internal Medicine, as well as Examination and Certificate procedure, will be considered.

It now seems probable that the first (Part I) Written Examination will be held in December, 1936, and the first (Part II) Practical or Clinical Examination will be conducted at or near the time and place of the Annual Session of the American College of Physicians in 1937.

The Joint Committee at this time desires to record its appreciation of the constant encouragement and valuable advice given so freely at all times by Dr. James Alex. Miller, President of the American College of Physicians, Dr. William J. Kerr, Chairman of the Section on Practice of Medicine of the American Medical Association, and particularly Mr. E. R. Loveland, Executive Secretary of the American College of Physicians, for many important suggestions and faithful coöperation during the formative period of the American Board of Internal Medicine.

Respectfully submitted—WALTER L. BIERRING, *Chairman*

JONATHAN C. MEAKINS O. H. PERRY PEPPER WM. S. MIDDLETON DAVID P. BARR JOHN H. MUSSER G. GILL RICHARDS	*American College of Physicians*	ERNEST E. IRONS REGINALD FITZ WALTER L. BIERRING	*Section on Practice of Medicine, American Medical Association*

In submitting this report, Dr. Bierring asked members of the Board to read the material over carefully in preparation for a further discussion of the matter at the next meeting. Dr. Bierring's report was received with applause and a resolution adopted accepting the report with the profound thanks of the Board of Regents. Thereupon, Dr. Bierring stated that the formation of this Board has gone forward in stages, and that his Committee feels that at this time the steps that have been taken thus far should have the sanction of the Board of Regents of this College. It was suggested, however, that action be deferred until after the reports might be further studied and also examined by the Board of Governors.

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE BOARD OF REGENTS

DETROIT, MICH.

March 3, 1936

The second meeting of the Board of Regents, during the Twentieth Annual Session at Detroit, was held Tuesday, March 3, 1936, at the Book-Cadillac Hotel, convening at 12:15 o'clock, with Dr. James Alex. Miller, President, presiding; with the following present: James Alex. Miller, President; Ernest B. Bradley, President-Elect; Arthur R. Elliott, First Vice-President; David P. Barr, Second Vice-President; William Gerry Morgan, Secretary-General; William D. Stroud, Treasurer; Walter L. Bierring, John H. Musser, O. H. Perry Pepper, Luther F. Warren, William J. Kerr, Roger I. Lee, Sydney R. Miller, George Morris Piersol, G. Gill Richards, James B. Herrick, Jonathan C. Meakins, James H. Means, James E. Paullin, Maurice C. Pincoffs, Charles H. Cocke, and with Mr. E. R. Loveland, Executive Secretary, acting as secretary of the meeting.

The reading of abstracted Minutes of the previous meeting was dispensed with.

Dr. Charles H. Cocke, Chairman of the Board of Governors, reported the following resolutions received from the Board of Governors at their meeting the day previous:

RESOLVED, that the Board of Governors recommend to the Board of Regents, and such other Officers as may be concerned in the selection of the time for the Annual Meeting, to hold future Annual Sessions at as late a date in April as consistent with the convenience of those in the City in which the meeting will be held.

Chairman Miller ruled that this resolution merely will be entered on the Minutes as a record of a communication to be considered by those in charge of setting the date of the next meeting.

RESOLVED, that the Board of Governors suggests to the Board of Regents the desirability of having the By-Laws amended to provide for the appointment of alternates for Governors who cannot attend the Annual Sessions.

It was explained by Dr. Cocke that there were three proxies allowed to sit by unanimous vote of the Board of Governors at the meeting of that Board the preceding day. He felt that every constituency has a right to representation, and since there is no constitutional provision for it, the Board of Regents should take under consideration proper amendments providing for the same.

On motion by Dr. Piersol, seconded by Dr. Bradley, and regularly carried, it was

RESOLVED, that the Board of Regents instruct the Committee on Constitution and By-Laws to draw up proper amendments providing for alternates for Governors who cannot attend the Annual Sessions, and that the proposed amendments be presented in accordance with present provisions of the Constitution and By-Laws.

RESOLVED, that the Board of Governors shall express to the Board of Regents their approval of the project for the acquisition of a permanent College home and headquarters, and, further, recommend that the Board of Regents proceed immediately on the project.

Chairman Miller reported that he had been present at the meeting of the Board of Governors at which the matter of the College Headquarters was discussed, and that it was quite impressive, since it was unanimous, with the exception of one Governor, in revealing what the general fellowship of the College feels about it. There had not been a single vote from the Board of Governors in the negative, although in the discussion at least one had indicated some opposition.

RESOLVED, that the Board of Governors express to the members of the Board of Regents their keen appreciation and thanks for the Dinner tendered them on March 1.

It should here be recorded that the members of the Board of Regents, as individuals, tendered a Dinner to all members of the Board of Governors who could be present on the evening preceding the opening of the Annual Session. Matters of general interest to the College and to each Board were freely discussed.

Chairman Miller reviewed the present status of the situation regarding the College

Headquarters, explaining that to date the Board had had only a committee headed by Dr. Stengel who had reported informally upon preliminary possibilities. Now, with this resolution from the Board of Governors, one of the possible obstacles to this serious project had been removed. He asked for the judgment of the Board as to how best to proceed in the matter. He stated that he would make reference to it in his annual address at the Convocation and that the matter could be further mentioned at the Annual Business Meeting on March 5.

Dr. O. H. Perry Pepper expressed the opinion that it would be proper to appoint a new committee to study the matter in detail, outlining it, get actual plans and actual estimates, but that that committee should not be empowered to proceed with the purchase of land or the erection of a building without further action by the Regents.

Chairman Miller explained that the committee that had been functioning thus far was appointed purely for a preliminary survey, that its work had probably been completed and that it might now be discharged with thanks.

Dr. Stroud, Treasurer of the College, being asked for comments, expressed his approval of the idea of appointing a new committee, but suggested further that there should be included within the motion authorization for any financial outlay from the College funds as may be necessary for the services of an architect, etc.

Upon motion by Dr. Bierring, seconded by Dr. Lee and regularly carried, it was

RESOLVED, that the temporary Committee on the College Headquarters be discharged with an expression of the deep thanks and appreciation of the Board of Regents for their general survey of the situation.

Chairman Miller pointed out that if it be the wish of the Board of Regents, the Board might proceed to definite plans for the acquisition of a new home and authorize the appointment of a definite committee for making concrete plans, and also to inform the Treasurer of such plans, because that might materially influence the disposition of funds that are now idle awaiting reinvestment.

In the discussion that followed, it was brought out that this might mean that the new committee would be authorized, if they felt wise, to employ an architect and to prepare definite plans. The committee would look into the particular proposition presented by the previous committee in Philadelphia and would also consider other suggestions concerning Washington, or any other city, but the Board of Governors were unanimous in expressing a preference for Philadelphia. The report of the new committee at the next meeting of the Board of Regents would have to be a very businesslike affair, not informal and not indefinite.

On motion by Dr. Bierring, seconded by Dr. Bradley and regularly carried, it was

RESOLVED, that the incoming President shall appoint a Committee on College Headquarters which shall be authorized by the Board of Regents to proceed actively at once with detailed plans for the acquisition, or the construction, of a new College Headquarters, including the selection of a suitable site, the selection of the proper city, and, further, with authorization for preliminary expenditures for an architect, and with instructions to report to the Treasurer as to any financial arrangements entered into, so that proper funds may be available.

The report of this committee shall be presented to the Board of Regents as soon as feasible—a special meeting of the Board of Regents or the Executive Committee may be called if deemed advisable.

Dr. Maurice C. Pincoffs, Editor of the ANNALS OF INTERNAL MEDICINE, made a brief report to the effect that his work had been greatly aided by the temporary appointment of Dr. Clough. Before another meeting he expressed the hope that that appointment may become permanent. He had been receiving a satisfactory number of manuscripts. The papers presented at the Annual Meeting remained the backbone of the publications in the ANNALS, and probably always will. He reported that unfortunately his office had gotten behind some weeks in getting out the journal recently. He expressed the assurance that the condition would be corrected.

In the absence of Dr. Charles F. Martin, Chairman of the Committee on Finance, Dr. Roger I. Lee presented the following report, which, upon motion, was accepted and filed:

"Your Finance Committee beg to report a very satisfactory condition of the annual budget. Detailed statement of this will be given by the Treasurer at the appropriate time.

"They would draw attention to the fact that more than half of the gross income of $72,000 is derived not from dues from members (which represents only $31,000), but from the exhibits, subscriptions to the ANNALS, advertisements in the ANNALS and other minor sources of income.

"Attention has been directed, from time to time, to the substantial annual surplus of the organization in recent years. On the other hand, your Committee would remind the Board of Regents that the income from the ANNALS and its advertisements is always a variable quantity according to the size of the ANNALS, the price of paper and printing, the cost of labor and the amount of advertising obtained,—that furthermore, an urgent need exists for more space in the executive offices, perhaps an increase in the personnel of the central office and an expense to be incurred through underwriting the Certification Board,—in all of which instances, increased demands will be made on the annual budget.

"Your Committee approves the budget for 1936 as presented in the financial report of 1935.

"Initiation Fees and Annual Dues: In order to correct false impressions, they would remind the Regents, as well as the Fellows generally, that the initiation fee has been reduced to $80, and that the annual dues of $15 include the Journal.

"They would recommend that an entertainment allowance for the President of $200 be set aside in the budget to be drawn upon if, as and when required for special occasions.

"It will be of interest to the Regents to know that the book value of securities today, in comparison with that of the original cost, will bring an enhancement of the values of securities and equities equivalent to approximately $7,000.

"The Finance Committee feels a responsibility with respect to your investments and suggests that a Trust Company, to be selected after due consideration by the President and Treasurer, be employed to act as agent to supervise the accounts of the College and advise with regard to investments, giving such suggestions to the Finance Committee as is dictated by their expert judgment. They recommend that such a service be obtained from the best Trust Company in Philadelphia at a figure commensurate with the amount of capital involved—this service not to exceed, perhaps, $300 per year.

"Respectfully submitted,

"(Signed) C. F. MARTIN,
"*Chairman, Committee on Finance*"

Dr. Stroud, Treasurer, explained that the handling of the investments is a heavy responsibility, and that it is difficult for the Committee on Finance to keep up with the rapidly changing ideas in investment principles. College funds could be better and more safely invested if such counsel were available. The responsibility for purchases and sales would still be with the Finance Committee, the investment counsel merely being an assistant agency in helping the Committee.

Upon motion by Dr. Pepper, seconded by Dr. Lee, and regularly carried, it was

RESOLVED, that an appropriation of $300.00 be added to the 1936 budget in accordance with the recommendation embodied in the last paragraph of the Finance Committee's report.

Another item in the report requiring special consideration was the recommendation of the establishment of a fund of $200.00 for the President's Entertainment Fund. Dr. Lee, in commenting upon the matter, pointed out that it is a very modest sum, and the financial responsibilities that are indirectly put upon the President may in some instances be very large, and it seemed to the Finance Committee, despite the opposition of the President, that a moderate allowance was fitting for such an organization as the College to provide. Dr. Pepper, another member of the Committee, pointed out that the word "special" in the

report does not mean occasions other than those which may arise and always do arise at the Annual Meeting. In other words, it refers only to the usual entertainment incident to the Annual Meeting.

Upon motion by Dr. Piersol, seconded by Dr. Herrick, and regularly carried, it was

RESOLVED, that the sum of $200.00 be appropriated for the year 1936–37, in accordance with the sixth paragraph of the Finance Committee's report.

Dr. William D. Stroud, Treasurer, distributed mimeographed copies of the annual report, which hereafter follow, and commented as follows:

> "The annual report now in your hands explains the financial situation of the College. Mr. Loveland's report on page 1 shows that we have an Endowment Fund of $58,281.72 and a General Fund of $99,047.47; total assets of $157,329.19. On our investments the total purchase price of our bonds is $111,844.82, while an estimate of their sale value on February 28, 1936, taken from quoted prices, was $116,130.15, an appreciation of more than $4,000.00. The purchase price of our stock was $14,811.00, which are now worth at current prices, $17,902.00, therefore with an appreciation of over $3,000.00. The total appreciation on bonds and stocks is therefore in excess of $7,000.00."

Upon motion by Dr. Cocke, seconded by Dr. Lee, and regularly carried, it was

RESOLVED, that the report of the Treasurer be accepted and filed.

Chairman Miller pointed out that the budgets for the year 1936 had already been presented and passed upon by the Board of Regents at their meeting in Philadelphia, December 15, 1935, except for the two additions authorized at this meeting.

The report from the Committee on Fellowships and Awards, headed by Dr. David P. Barr as Chairman, was deferred for a later meeting.

Dr. Walter L. Bierring, Chairman of the joint Committee on the Certification of Internists, reported that the Committee had held one meeting during this Session, and, in a tentative way, had added a few facts to what was reported previously. No special meeting of the Committee is planned at the Kansas City Session of the American Medical Association, except of those members who are required to bring the matter before the Section on the Practice of Medicine. It was contemplated that the first meeting of the American Board of Internal Medicine will be held during the first week in June for the purpose of working out further details (henceforth the joint Committee on the Certification of Internists will be referred to as the "American Board of Internal Medicine"). The Committee felt that one of its great problems will be the determination and selection of the Founders' Group.

Dr. O. H. Perry Pepper, a member of the Committee, expressed the suggestion that the Founders' Group might be built up very slowly. The determination of the Founders' Group must be based upon definite principles yet to be developed. Those selected must be men about whom there could be no question or criticism. Other opinions and plans were suggested by Dr. Meakins, also a member of the Committee.

On motion by Dr. Herrick, seconded by Dr. Pepper, and regularly carried, it was

RESOLVED, that the Board of Regents of the American College of Physicians approves of the plan of the Committee on the Certification of Internists as outlined for the American Board of Internal Medicine, and the Board of Regents authorizes its representatives on said Board to proceed, using their best judgment.

There was general discussion about any appropriations needed for the operation of the Committee before the next meeting of the Board of Regents. It had been pointed out that the Board of Regents had originally authorized the financing of this project to the limit of $10,000.00, but that only $1,000.00 specifically has been budgeted.

Upon motion by Dr. Pepper, seconded by Dr. Bradley, and regularly adopted it was

RESOLVED, that the Board of Regents shall appropriate a sum of $4,000.00 additional, total $5,000.00, on the 1936 budget to be made available, if necessary, for the American Board of Internal Medicine.

There was some discussion about a special meeting of the Board of Regents to be held for a final report from the Committee on College Headquarters and also from the American Board of Internal Medicine. The matter was left open, subject to the call of the President when such reports are ready and action necessary.

Dr. John H. Musser stated that he could not be present for the meeting of the Board of Regents on Friday, March 6, but wished to present to the Board an invitation for the Annual Session of 1938 to be held in New Orleans. An official invitation is being prepared by New Orleans, and will be sent to the Executive Secretary. He pointed out that just as the Twentieth Annual Session has been held in Detroit ten years following its previous meeting, the Twenty-second Annual Session, if held in New Orleans, would also be ten years after the previous meeting.

Chairman Miller asked Dr. Musser if it would make any difference particularly to New Orleans whether the College came in 1938 or 1939, inasmuch as New York City also had been planning for sometime to present an invitation for 1938. Dr. Musser replied that it will not, except for reasons of sentiment.

Dr. William J. Kerr at this point presented a memorial prepared by Dr. C. E. Watts, Governor of the College for the State of Washington, on the death of Dr. Frederick Epplen, for many years the College Governor for Washington.

On motion by Dr. Kerr, seconded by Dr. Bierring, and regularly adopted, by rising vote, it was

RESOLVED, that the following tribute be recorded in the Minutes of the Board of Regents, that a copy be transmitted to Mrs. Epplen, and that this memorial be published in the ANNALS OF INTERNAL MEDICINE.

IN TRIBUTE TO DR. FREDERICK EPPLEN

"The Philadelphia Session last year was attended by Dr. Frederick Epplen, who had been a member of the Board of Governors for many years. The question of his attending that last Session had been carefully considered and debated. He knew well that the trip to Philadelphia would cost him a large proportion of the myocardial compensation he possessed, but he felt sure that it would be the last opportunity of his lifetime. He elected to exchange most of his remaining strength and probably a part of the days left to him for the joy of association, the renewal of friendship, the revival of memories, in the College. Within the month he died, suddenly as he wished it, because he dreaded a lingering death.

"And thus passed one who was loved by all of us. He was not a prolific author, and yet he was well known the country over. By birth, training at home and abroad, and life long habit, his approach to medicine was intensely scientific rather than artful. He was rewarded with an unusually large practice for many years. The pressure of this professional work did not prevent him from maintaining his contacts and friendships in various organizations, especially in the College.

"The elevation of the level of medical practice in the Pacific Northwest was his constant desire. He gave much time and effort to the Pacific Northwest Medical Association, and the success of this adventure in postgraduate training stands as a tribute to him. A

firm believer in the County Medical Society as a disseminator of facts and ideas, he attended its meetings regularly, and he organized special societies in internal medicine, study clubs and discussion groups where needed.

"As a means for the advancement of internal medicine and for improvement of all medicine, he believed thoroughly in the College of Physicians. His best efforts were given in its behalf. He acted as Governor for Washington for many years, and worked diligently in that capacity. He rarely failed to attend the Annual Sessions, and his friendships in the College were cherished as none other.

"During the last four years it was distressing to his friends to see him failing, and to have a cessation of activity in one who had been so energetic. Yet it was inspiring that his enthusiasm never waned, and his final effort to participate in the activities of the College was so characteristic of him and of what he held in highest esteem, that the memory of him will be with us always."

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE BOARD OF REGENTS

DETROIT, MICH.

March 6, 1936

The third meeting of the Board of Regents during the Twentieth Annual Session was held on March 6, 1936, at the Book-Cadillac Hotel, Detroit, convening at 12:20 o'clock, with President Ernest B. Bradley presiding, and with the following present: Ernest B. Bradley, President; James H. Means, President-Elect; David P. Barr, Second Vice-President; William D. Stroud, Treasurer; William Gerry Morgan, Secretary-General; James Alex. Miller, Francis M. Pottenger, Luther F. Warren, William J. Kerr, Roger I. Lee, George Morris Piersol, G. Gill Richards, Jonathan C. Meakins, Maurice C. Pincoffs, James D. Bruce, and with Mr. E. R. Loveland, Executive Secretary, acting as secretary of the meeting.

Upon motion, seconded and regularly carried, the reading of the Minutes of the previous meeting was dispensed with.

On motion by Dr. J. A. Miller, seconded by Dr. Stroud and regularly carried, it was

RESOLVED, that the President appoint a committee to revise and rewrite the present Fellowship Pledge of the College.

President Bradley appointed Dr. James H. Means, of Boston, a committee of one, to carry out the resolution.

President Bradley next brought up the matter of constitutional provisions for the endorsement of candidates either by a Governor, an Officer or a Regent. Although none of these may propose a candidate, some members of the Board of Governors have felt that it should be the policy of Officers and Regents to refrain from endorsing a candidate, so that all candidates may pass through their hands for investigation and final endorsement. Furthermore, President Bradley suggested that it might be more acceptable to the Committee on Credentials to have candidates endorsed by their respective Governors rather than Officers and Regents.

After general discussion, during which it was brought out that whether or not a proposal is endorsed by the Governor, it is always referred to the Governor by the Executive

Secretary, and the Governor given an opportunity to file his report before action by the Committee on Credentials, on motion by Dr. James Alex. Miller, seconded by Dr. Means and regularly carried, it was

RESOLVED, that it is the sense of the Board of Regents that for the present at least it be considered desirable for no Officer or Regent to act as endorser of candidates, but rather that all proposals be referred to the Governor for the district from which the candidate comes.

This resolution did not carry with it a recommendation of the changing of the By-Laws, which provide that an Officer or Regent may endorse a candidate as well as a Governor. The purpose of the resolution was merely to try out the plan of having all candidates endorsed officially by the Governor, so that in no case would the Governor be overlooked.

The Executive Secretary, Mr. Loveland, presented two communications from Dr. James D. Bruce, Governor for Michigan, recommending the reinstatement to Fellowship in the College of Dr. Eva Finn and Dr. William Clift, who had resigned five or six years ago. Their reinstatement was recommended by Dr. Bruce in accordance with their desire to pay up past dues rather than being reproposed as new cases.

On motion by Dr. Pottenger, seconded by Dr. Lee and regularly carried, it was

RESOLVED, that Dr. Eva Finn and Dr. William Clift be reinstated as Fellows of the College subject to the payment of the dues from the time of their resignations to date.

President Bradley at this time pointed out that the Constitution of the College permits specialists in other lines than Internal Medicine to become Fellows, such as roentgenologists, pathologists, pediatricians, neurologists, psychiatrists and others. There has been a growing tendency toward limitation of membership to those engaged in Internal Medicine. However, if such limitation shall be carried out, it will be plainly necessary to amend the Constitution and By-Laws. This could not affect those who are already members of the College, but would change the policy in connection with the election of new members in following the specialty of Internal Medicine.

The Executive Secretary then presented the following communication and resolution from the Board of Governors, as adopted at their meeting on March 5:

RESOLVED, that the Board of Governors suggest to the Board of Regents that each year the Executive Secretary send out appropriate questionnaires to obtain information as to the status and work that the members of the College have done during the preceding year, and that these records should be kept on file in the headquarters office.

Later in the Minutes of the Board of Governors particular reference is made to Associates. The motion was intended to include all members of the College, but particularly Associates. The Board of Governors, in their discussion, felt that there should be available up-to-date information about every member of the College, what he has done during the past year, his contributions, his new appointments, etc.; they also felt that it would be a stimulus to Associates who are attempting to qualify for Fellowship for the College office to be following them up concerning these data each year.

The Executive Secretary explained that this motion was initiated by some Governors of the College who had inquired for specific information concerning what certain physicians had done during the last two or three years. It not only was not available in the College, but could not be procured through the American Medical Association, or elsewhere. These men feel it desirable to have this information available in the College office about every man.

Dr. Bruce, speaking to the question, explained that a plan of this character had been employed at the University of Michigan with reference to postgraduate work for the past six years, and that he now has at his office in Ann Arbor the records of over three thousand of the Michigan State members concerning their attendance on various postgraduate activities, both within and out of the State. The plan has had a stimulating effect on the men. He recommended the idea as a very excellent one for the stimulation of Associates particularly.

Dr. James Alex. Miller made inquiry as to the amount of work such a plan would entail in the Executive Offices, whether it would require additional clerical service, filing equipment, etc. The Executive Secretary replied that the present staff could take care of the work without excessive burden, but that additional space and files would be required. The volume of

material on file grows tremendously in an organization of this character. Mr. Loveland further explained that there is an individual folder for every Fellow and Associate of the College. The records, however, are often meagre for those members who have been in the College for many years, for in many instances no original application forms, or, for that matter, any other relevant records were received from the early executives of the College. However, records are fairly complete for all members from about 1920 forward, and wholly complete from 1926 forward.

On motion by Dr. Lee, seconded by Dr. Pincoffs and regularly carried, it was

RESOLVED, that a committee be appointed to draw up a plan for the sending out of blanks which will keep the College records up to date concerning the accomplishments of its Fellows and Associates, the committee to report back at the next meeting.

President Bradley subsequently appointed the following committee:

James D. Bruce, Chairman
Jonathan C. Meakins
Maurice C. Pincoffs

In the discussion, it was brought out that these blanks are intended primarily to keep the College records up to date as to the accomplishments of our Fellows and Associates, that the first records at least shall be complete for a man's entire history, and that the annual form sent out thereafter shall be intended merely to supplement the original record.

Dr. James Alex. Miller proposed that inasmuch as the formation of the American Board of Internal Medicine and the activities of other committees, such as that of the Committee on Credentials, will affect the constitutional requirements for admission to the College, that the Committee on Constitution and By-Laws review and, perhaps, present proper amendments at the next meeting of the Board of Regents. He pointed out that our Constitution says that Fellows shall be members of the medical profession engaged as practitioners, teachers or research workers in Internal Medicine or in an allied specialty. Perhaps the last clause should be deleted.

President Bradley pointed out that in the appointment of new committees due consideration will be given to overlapping certain appointments, so that the Committee on Constitution and By-Laws will have a better appreciation of any amendments that may be necessary.

On motion by Dr. J. A. Miller, seconded by Dr. Richards and regularly carried, it was

RESOLVED, that there be referred to the Committee on Constitution and By-Laws a request for a report and suggested changes in the Constitution and By-Laws to meet the new demands of the College standards for qualification for Internal Medicine.

Dr. Miller's motion had in mind the preparation of such amendments as may be made necessary by the further restriction of the College membership to internists, as may be occasioned particularly by the operation of the new American Board of Internal Medicine.

The next matter of business was the election of a Secretary-General and of a Treasurer for 1936–37.

Dr. George Morris Piersol nominated Dr. William Gerry Morgan for reëlection; Dr. Luther F. Warren seconded the nomination.

President Bradley called for other nominations, of which there were none.

Dr. William Gerry Morgan was unanimously elected Secretary-General for the year 1936–37.

Dr. George Morris Piersol nominated Dr. William D. Stroud for reëlection as Treasurer; Dr. J. A. Miller seconded the nomination.

By motion seconded and regularly carried, nominations for Treasurer were closed.

Dr. William D. Stroud was unanimously elected Treasurer for the year 1936–37.

On inquiry by a member of the Board, it was disclosed that the Treasurer is bonded in the amount of $50,000.00.

Dr. David P. Barr, Chairman of the Committee on Fellowships and Awards, reported for that Committee, reading a letter from Dr. John P. Peters concerning Dr. Michael J. Lepore, who is the American College of Physicians Research Fellow at Yale University for

1935–36. Dr. Peters' letter revealed that he considers the granting of these fellowships as the most worthy thing the College carries on. Dr. Lepore's work was reported on in detail, with most favorable comment.

Dr. Barr then reported that the Committee recommends to the Board of Regents the appointment of Myron Prinzmetal as Research Fellow for 1936–37. Dr. Prinzmetal was graduated in 1932 from the University of California. His record in school was extraordinary. He worked in the Department of Pharmacology, the Department of Pathology and the Department of Medicine as a student and in each of these did investigative work of high order. Two years ago he was appointed National Research Fellow; letters from his former teachers were of the most enthusiastic kind. Dr. Barr stated that his Committee believed that Dr. Prinzmetal was considered the outstanding graduate not only of his year, but, perhaps, for five years. He later went to the Barnes Hospital, St. Louis, for a year as Assistant Resident, where he took part in some of the researches conducted by Dr. Kountz. He then went to the Boston City Hospital under Dr. Soma Weiss. As a result of the work with Dr. Weiss, he published a paper, "The Nature of the Peripheral Resistance to Arterial Hypertension, with Special Reference to the Vasomotor System." Dr. Barr passed a reprint of this publication around for examination by the Board. Dr. Prinzmetal had published about twenty-four papers even preceding the one in question, most of his publications in association with men from the various schools in which he had worked.

Dr. Barr stated that he was familiar with most of Dr. Prinzmetal's publications, and stated that he (Dr. Prinzmetal) had contributed much more than the ordinary assistant does contribute to researches with older men. The Committee is informed Dr. Prinzmetal wishes to pursue further work with Sir Thomas Lewis in London, especially to continue research on hypertension. The Committee, therefore, recommended to the Board of Regents Dr. Prinzmetal's selection for the Research Fellowship for the year 1936–37.

Upon motion by Dr. Lee, seconded by Dr. Meakins and regularly carried, it was

RESOLVED, that Dr. Myron Prinzmetal be awarded the Research Fellowship of the American College of Physicians, amounting to $150.00 per month for twelve months, beginning July 1, 1936.

Dr. Stroud inquired whether in view of the fact that some felt there should be additional fellowships, Dr. Michael J. Lepore now working at Yale University and whose fellowship expires in June might not be considered for an additional year.

Dr. Barr, for the Committee on Fellowships and Awards, reported that Dr. Lepore had not requested a continuation of his fellowship, and expressed the belief that Dr. Lepore might be provided for directly in the budget at Yale. Dr. Barr expressed a doubt as to there being any necessity the present year to consider the extension of his fellowship. He said further that in appointing a Fellow the College assumes at least a great interest in that man and a certain degree of responsibility for seeing that he has the opportunity to develop from this grant, and when and if the College funds permit the extension of fellowships in this form or in other forms, the matter should be actively considered by the Regents.

Dr. Barr was informally authorized by President Bradley to write Dr. Peters, thanking him for his report on the work of Dr. Michael J. Lepore, and to convey to Dr. Peters the very great interest of the College in Dr. Lepore's work; also to find out, without in any way committing the College, what provision is being made for Dr. Lepore next year.

Dr. Richards inquired from Dr. Barr whether in his opinion the College would accomplish more good by extending a fellowship for two years, or to award separate fellowships to different men.

Dr. Barr's reply was that he feels that one year is preferable, because each one of these fellowships is, to a degree, a gamble; it cannot be determined how the one selected will succeed; in one year he has an opportunity of showing how good he is; if he is very good, the College, perhaps, should consider him for a second year.

Dr. James Alex. Miller: "Mr. President, in this connection, following up the line on which I spoke at the General Business Meeting yesterday, it does seem to me that we ought to be thinking over, in connection with our plans for a new home, also the question of a

program for possibilities of using surplus funds for the advancement of Internal Medicine. This granting of Fellowships would be one method; there may be others. It seems to me that it would be very helpful if, in addition to your specific committee that has already been authorized for the consideration of specific plans and estimates for our new home, we had at the same meeting a report from another committee that might consider other possibilities for a program of funds, with some estimate of what that would involve, which would help us to determine another thing; that is, this question as to in what way, if any, we should reduce the financial obligations of the new Fellows. It seems to me that it might help in this whole matter if we at this meeting authorize the appointment of another committee to report at the same time that the House Committee does, in connection with the possibility of a future program for the use of available funds of the College for the promotion of Internal Medicine, leaving it open to more fellowships or something else.

"Dr. Pincoffs made the suggestion of some sort of revolving fund and some of us have been discussing a revolving fund that might be given to young men, that would be turned back. If it was similar to other revolving funds, it might be of great value to this organization. That money would very likely come back, come back to us with interest.

"In other words, there is quite a field there and I think that while we are considering this new home, the Fellowship of the College would be very much interested to know how much we have been considering other possible programs for the use of our money and, if they could consider them altogether, it would seem to me it would be very helpful."

In the discussion that followed, Dr. Miller indicated that this additional program would not be limited to fellowships and awards alone, but that there should be some committee to take up a composite program that would include everything that the College might consider.

Dr. Kerr said that as soon as the American Board of Internal Medicine is established and begins to function, queries will probably begin to come in as to facilities for training as internists in this country. The College should be prepared to furnish such information about these facilities both in this country and abroad. He suggested that the College might definitely consider the investment of some of its funds in assisting young men who cannot afford to continue their training as they should. But, the College should be well informed and be well prepared, through a survey, before launching on any particular project.

On motion by Dr. Pincoffs, seconded by Dr. Barr and regularly carried, the following resolution was adopted:

RESOLVED, that a Committee on Future Policy for the development of Internal Medicine be appointed by the President for the purpose of considering a program of possibilities for using surplus funds for the advancement of Internal Medicine. This committee shall take under consideration all matters outside of that of the College Headquarters, such as fellowships, awards, postgraduate education, initiation fees of new Fellows, revolving funds for the aid of research, etc.

President Bradley subsequently appointed the following Committee:

James Alex. Miller, *Chairman*
Walter L. Bierring
Roger I. Lee
Maurice C. Pincoffs
Francis M. Pottenger

The following Executive Committee of the Board of Regents was elected for the year 1936–37:

Ernest B. Bradley, *Chairman*
James H. Means
William Gerry Morgan
William D. Stroud
Walter L. Bierring
Roger I. Lee
James Alex. Miller
Maurice C. Pincoffs
Francis M. Pottenger

President Bradley proceeded to the appointment of committees in accordance with the Constitution and By-Laws or special regulations previously adopted by resolution by the Board of Regents (asterisk indicates new appointment; x indicates reappointment).

Committee on Advertisements and Commercial Exhibits

xE. J. G. Beardsley, *Chairman*
xGeorge Morris Piersol
xWilliam D. Stroud

* * * * *

Committee on Annals of Internal Medicine

xJames H. Means, *Chairman*	(1939)
David P. Barr	(1938)
*Egerton L. Crispin	(1937—taking the place of O. H. Perry Pepper, resigned)

* * * * *

Committee on Fellowships and Awards

xDavid P. Barr, *Chairman*
*Jonathan C. Meakins
xJames H. Means
xWilliam J. Kerr
*Hugh J. Morgan

* * * * *

Consulting Committee on Annual Sessions

Ernest B. Bradley, *Chairman*
David P. Barr
James Alex. Miller
Jonathan C. Meakins
Alfred Stengel

The Consulting Committee on Annual Sessions is automatic in its appointments, being made up of the President and General Chairman of the current and last two sessions.

Committee on Constitution and By-Laws

Jonathan C. Meakins, *Chairman*	(1938)
Alfred Stengel	(1937)
*James B. Herrick	(1939)

* * * * *

Committee on Credentials

Representing the Board of Regents:

*Sydney R. Miller, *Chairman*	(1939)
Luther F. Warren	(1938)
George Morris Piersol	(1937)

(The three representatives appointed by the Board of Governors included):

William B. Breed	(1937)
Charles H. Cocke	(1938)
*J. Owsley Manier	(1939)

* * * * *

Committee on Finance

*James Alex. Miller, *Chairman*	(1939)
O. H. Perry Pepper	(1938)
Roger I. Lee	(1937)

* * * * *

Committee on Nominations

George Morris Piersol, *Chairman*	(from the Board of Regents)
James D. Bruce	(from the Board of Regents)
William B. Breed	(from the Board of Governors)
Charles T. Stone	(from the Board of Governors)
Charles F. Martin	(Member-at-Large)

* * * * *

Committee on Public Relations

*James E. Paullin, *Chairman*	(1939)
*Robert A. Cooke	(1940)
Walter L. Bierring	(1937)
James F. Churchill	(1938)

Ex Officio

Ernest B. Bradley

Committee on Certification of Internists

(American Board of Internal Medicine)

This Committee remains as previously appointed:

Walter L. Bierring, *Chairman*	(A. M. A.)
Reginald Fitz	(A. M. A.)
Ernest E. Irons	(A. M. A.)
James H. Means	(A. M. A.)
David P. Barr	(A. C. P.)
Jonathan C. Meakins	(A. C. P.)
William S. Middleton	(A. C. P.)
O. H. Perry Pepper	(A. C. P.)
G. Gill Richards	(A. C. P.)

* * * * *

Committee on College Headquarters

Roger I. Lee, *Chairman*
O. H. Perry Pepper
William D. Stroud
James Alex. Miller
David P. Barr

The Executive Secretary then presented invitations for the 1937 Annual Session from the Cities of Columbus, Buffalo, Cleveland, Toledo, Memphis and St. Louis, including one for 1938 from New Orleans. The two most complete invitations were from Memphis and St. Louis, and were read in detail. They contained official invitations from all the medical organizations, the medical school, civic bodies, hotels, Chamber of Commerce, the Governor for the State, the local Regent and Fellows, and others.

On motion by Dr. J. A. Miller, seconded by Dr. Piersol and regularly carried, it was

RESOLVED, that the Twenty-First Annual Session of the American College of Physicians be held in St. Louis during 1937.

On motion by Dr. Barr, seconded by Dr. Richards and regularly carried, it was

RESOLVED, that the date of the meeting shall be during the third week of April, namely, April 19–23, 1937.

Dr. James Alex. Miller reported that he has been discussing with keymen in New York City the possibility of the College coming to New York in 1938, and expressed the opinion that there will undoubtedly be a complete invitation laid before the College for the 1938 Session.

On motion by Dr. Meakins, seconded by Dr. J. A. Miller and regularly carried, it was

RESOLVED, that Dr. David P. Barr shall act as the General Chairman of the 1937 Session in St. Louis.

Dr. G. Gill Richards inquired why the Daily Bulletin had been discontinued at the 1936 Session, saying that several inquiries had come to him from members in attendance who missed the Bulletin.

The Executive Secretary, Mr. Loveland, reported that the Daily Bulletin had never been officially established by the Board of Regents, but had been published by him primarily for the exhibitors. It had entailed a tremendous amount of work because each issue had to be published over night with a great deal of work in preparing copy, proof reading, etc. Furthermore, its publication had entailed an expense of from three to four hundred dollars. He said that the bulletin was not serving any valuable purpose so far as exhibitors were concerned. The daily registration of attendants at the Session is of some value, but will be furnished to exhibitors after the meeting. He reported that the Editor of the ANNALS had preferred not to act as editor of the Daily Bulletin, and it had been discontinued at the Detroit meeting purely because of the burden of work entailed by its publication.

President Bradley asked for the opinion of the Board of Regents, saying that if they felt it worth while, the Executive Secretary would be glad to publish it.

On motion by Dr. Piersol, seconded by Dr. J. A. Miller and regularly carried, it was

RESOLVED, that the publication of the Daily Bulletin at the Annual Sessions be discontinued because of the amount of work and the expense attached.

President Bradley, speaking about the present Session and the one for 1937, informed the Board of Regents that he would like to have a free expression of recommendations and suggestions for the program next year. He stated he had talked with many of the members of the College about the program of the Detroit Session, and without a dissenting voice, the opinions had been that the program was excellently arranged. Sometimes addresses were considered too numerous for the time available at former meetings, but there had been no such criticism at the current meeting. He had also talked with the exhibitors, who expressed their appreciation of the forty-five minute intermissions in the General Sessions. Some of them felt that the program ran too late in the afternoon, and expressed the desire to have a little more time open for the inspection of exhibits. Exhibitors had expressed some question as to the desirability of his suggestion that the intermissions might be shorter with earlier closing in the afternoon. President Bradley stated that he felt it should be announced by every presiding officer on the afternoon session before intermission that this time is given attendants solely for their visit to and inspection of the exhibits, and suggested that this announcement be placed on the afternoon agenda in the future.

Dr. David P. Barr inquired if it were the feeling of the Board that it is necessary to have a considerable competition of clinical programs or a greater number of clinical programs each morning. He suggested the possibility that at St. Louis he might be able to arrange two, or at the most three, programs of high excellence, with halls sufficiently large to accommodate the people who wish to come, and inquired whether the Board felt that at the same time there should be a larger number of programs in other places. At some of the Sessions there are about twenty different clinics going on simultaneously.

President Bradley, referring to the didactic morning lectures at the Philadelphia Session, reported that the chairman of the clinics, Dr. Pepper, had found that they were rather popular among some of the men who did not wish to go hither and yon to various hospitals and laboratories for clinics. It was offered as a suggestion for consideration at the St. Louis meeting again. President Bradley said that he saw no particular reason why men should be sent to hospitals unless patients were to be shown and real clinics given.

Dr. Stroud inquired whether by doing this there might not be some danger of curtailing the attendance at the various clinics.

Dr. Lee expressed the opinion that it is merely a question of competing against one's self in either event. He personally had a strong feeling that the mornings are clinical sessions, but that there has been a strong drift against the clinical session in the hospital; yet these clinics are the real keynotes of the meetings and the members ought to be encouraged to go to the hospitals, otherwise the actual purpose of the College is defeated. He said further that the only criticisms he had heard were that the standard of both the clinics and the lectures should be raised, getting them out of the district medical society level to which they have drifted and getting them on the level of internists.

Dr. Meakins said that he had been very much impressed for quite a few years with the fact that the morning sessions, while they are supposed to be clinical, seldom provide patients. There have been lantern slides and x-rays. At his clinic that morning he had been the only one who had presented patients. The other patients were there, but were not used; they were left in the background and the speakers talked from slides, etc. The previous morning he had been at a dermatological clinic, and it had been most illuminating because they had something one can see. If the patient is not going to be used, if it is not going to be a real clinical program, why should the members of the College be put to the bother and trouble of going off to a distant hospital several miles away? Why should such presentations not be given at the headquarters?

Dr. Means stated that he heartily endorsed the sentiments of Dr. Meakins. He thought it very necessary to get back to the presentation of patients.

Dr. Pincoffs stated that he thought there are other features that could be developed that have been present at some of our meetings, one of which is the mornings at home for people in the laboratories. He referred especially to the Thorndike Laboratory in Boston, where this idea was well carried out. It was also carried out by a number of men in Philadelphia. Many men visiting those laboratories spoke highly of that feature.

Dr. Meakins further pointed out that if the College is to have real clinics it cannot have them in a place that seats two hundred people, because they can't see anything. Real clinics must be conducted in smaller groups.

President Bradley, in discussing the date of the next meeting of the Board of Regents, suggested that it might be necessary to call a meeting during the summer or the very early autumn, in order to receive reports from the Committee on the College Headquarters, the American Board of Internal Medicine and the Committee on Future Policy for the Development of Internal Medicine.

Adjournment.

Attest: E. R. LOVELAND,
Executive Secretary

VO

Hospital Library
36
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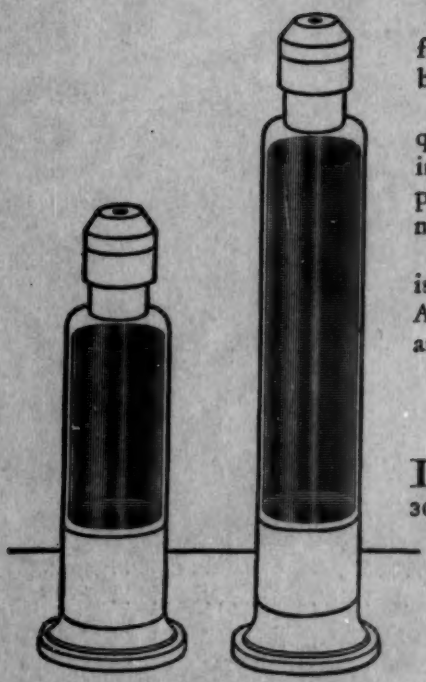

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O. H. Perry Pepper ..... Philadelphia
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